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FEDERAL SECURITY AGENCY
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12.7

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Approved by the Director, Bureau of the Budget, as required by Rule 42 of the Joint Committee on Printing

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription Price: Domestic 75 cents a year; foreign \$1.15

The Practitioner and the Antibiotic Age of Venereal Disease Control ¹

John H. Stokes, M. D.2

The succession of breath-taking, eyegoggling leaps with which the intelligence of man, his unguided demoniac, or his unwittingly unintelligent intelligence has covered space and time compressed into a chronologic instant of a decade or two is as much a reality in the field of medicine as in the physical sciences. We are in somewhat the position of the man in H. G. Wells' series of stories under the title of The Time Machine who discovered himself the possessor of an omnipotent wishing power and who, after a few preliminary passes, such as turning lighted lamps upside down, ordered the sun to stop. Bringing up on the lee side of a not yet uprooted rock, as all of civilization hurtled past him into dust with the cessation of rotation of the earth, he just managed in time to gasp a wish that everything be as it was before, and saved himself from Heaven knows what. can afford to give thought to his situation, as paralleled to no small extent by our own, and to utter a prayer for deliverance from Heaven knows what as events hurtle past us in the atomic and antibiotic age. For, as physicians, we stand at the edge of transformations which are as precipitous and even cataclysmic as the end of diagnostic medicine, the coming age of the pressure ampule and the self-treatment of disease, the twilight of the medical practitioner; unless indeed he can catch the ledge of psychosomatics or break his fall in the branches of the pediatric tree; or catch the gnarled roots of obstetrics or surgery as he plummets to oblivion.

My business is with but a single sector of this field of possibilities, in which the antibiotics have done things to us, DDT'd us into a disturbed, unstable biologic equilibrium, full of glow and promise, but with some ugly flickers and shadows here and there. Figure 1 summarizes the situation.

Figure 1.—What the antibiotics have done for venereal disease control

- 1. Provided almost ideally safe, reactionless, and increasingly inexpensive treatment for syphilis, gonorrhea, chancroid, and granuloma inguinale, with lymphogranuloma venereum next on the list.
- 2. Provided treatment so rapid that its duration is a matter of hours and (at most) days, instead of weeks, months, and years. This has abolished patient education in course, hampered contact tracing, weakened follow-up.
- 3. Provided treatment so rapid and simple as to make almost immediate reinfection a commonplace, and put free treatment in the position of subsidizing venery.
- 4. Relegated heavy metal and arsenic for practical purposes to the domain of the dodo and the moa.
 - 5. Put fever and the "hot box" into cold storage if not the scrap heap.

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¹Read before the Vancouver Medical Society on May 10, 1949.

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Figure 1.—What the antibiotics have done for venereal disease control— Continued

- 6. Provided safe and painless protection of the syphilitic mother and fetus—practically 100-percent effective for the fetus.
 - 7. Robbed congenital syphilis of its terrors.
- 8. Fallen just short of abolishing the reservoir of infectious syphilis and gonorrhea.
- 9. Put oral prophylaxis and the single-shot cure for what-have-you on the horizon—the tablet in the glass of whiskey, the pressure ampule dose in the thigh.
- 10. Returned the management of venereal disease to the practitioner if not to the patient himself. Effective self-treatment is just over the horizon.
 - 11. "Put the skids" under fear.

Where do the weak spots lie? In (2), (3), (8), (9), and (11). The only real answer is immunization.

Now let us turn in figure 2 to the objectives of epidemiologic control and attempt a simple and realistic statement.

Figure 2.—Objectives of epidemiologic control of venereal disease

- 1. To identify or uncover every infection, particularly in its transmissible stage; not only the infection itself but the "from whom, to whom" of it; recalling that every day's or hour's delay may mean a new infection.
- 2. To block infection transmission by methods of treatment which shall be quick (8 hours); lasting (as near no relapse and 100-percent cure as possible); reactionless; not too costly; not leave humanity in a worse state than before their application.
- 3. To use methods applicable by the practicing physician directly to the patient, with a minimum of assistance from without. Assistance means intermediation, loss of time, loss of privacy, increased cost.
- 4. To eliminate uncontrollable methods—self-treatment, across-the-counter prescribing, nostrums, quacks.
- 5. To educate for early recognition of disease before transmission, entrenchment, and treatment resistance occur.

Where are the weak spots? (1) "From whom, to whom," (2) the "worse state," (5) education for "early recognition."

Let us now turn the problem around on itself and consider the obstacles to epidemiologic control of the venereal diseases. Figure 3 presents another topical summary (my students used to call my dermatologic text book "the telephone directory").

You will easily see how formidable and

far reaching are the odds arrayed against us; how questionable indeed is even the immense power of antibiotic-implemented treatment to control and overcome these obstacles; how difficult are many of the crucial interpretations, such as those involving cure and relapse statistics and failure rates; and how strong is the temptation to heterodoxy, such as treatment on suspicion and treatment of the contact without diagnosis.

The amplification of these three résu-

Figure 3.—Obstacles to the epidemiologic control of the venereal diseases

Obstacle 1.—The tie-in with sex: a vital drive, undercover practice, money backing promiscuity and alcohol, the perennial fountainheads of venery.

Obstacle 2.—The stigma of venereal disease. Venereal disease is clandestine, will fight uncovering to the last ditch. It smears whatever it touches.

Obstacle 3.—Public and personal ignorance and lethargy. Try teaching people something they want to know for 25 years and see how slowly they learn. Then try teaching them something they don't want to know. Set the threshold of inertia and resistiveness at a minimal 65 percent.

Obstacle 4.—Medical unfamiliarity with venereal disease in all its aspects is now being made more serious by medical underestimation of the future problem. ("Penicillin has it in the bag." Now a common attitude.)

Obstacle 5.—Medical noncooperation. The doctor has too much to learn, too much to do, to master intricacies, elusiveness, and paper work.

Obstacle 6.—The subthreshold, asymptomatic onset of venereal disease and its initial period of unrecognized infectivity. If every patient upon infection ran a high fever with convulsions and a blazing rash, there would soon be an end of venereal disease.

Obstacle 7.—The carrier state. Conspicuous in gonorrhea, still a riddle in human, though recognized in animal experimental syphilis. Defeats recognition, maintains potential infectivity.

Obstacle 8.—Relapse and noncure. At a guess: for gonorrhea, 0 to 4 percent; for syphilis, 4 to 30 percent; for granuloma inguinale, 30 to ? percent; for lymphogranuloma venereum, ? percent. Maintains, with (6), (7), and (9), the reservoir of infection.

Obstacle 9.—Reinfection. Clinically unprovable, yet known to be frequent; an inevitable product of quick cure and no developed immunity; reinfection tangles all treatment-result and cure statistics, ping-pongs infections back and forth, sets the epidemiologic brain in a whirl.

Obstacle 10.—The mobile site and source of exposure. Contributions of gasoline and rubber, the automobile and facile transportation, have enormously complicated the control of the infected person.

Obstacle 11.—The approaching day of effective self-treatment. We must face the fact that the adequate treatment of venereal disease is getting less complicated than insulin; may soon join the aspirin category.

Obstacle 12.—The approaching day of treatment on suspicion, without diagnosis and without follow-up of results. To our generation, this is a hauling down of the flag of medical idealism and scholarship.

Obstacle 13.—The nonvenereal use of antibiotics. What will it do to the prevalence of venereal disease and the status of the suspected infectee?

Current indications place the toughest problems under (5), (6), (8), and (9).

més, topic by topic, would be material for a course rather than a single talk. I shall, therefore, confine myself to a discussion of ways and means by which the doctor can identify the infections that come his way; and some perhaps rather radical conceptions of what he might do when a venereal infection, a transmissible infection, is identified, or suspected.

Identification of the Infection, i. e., Case Uncovering

There are three golden moments in the public health control of the venereal infections: the moment when the patient comes before you with a suspicious complaint; the moment when a contact is named or described in identifiable terms; and the moment when, fortuitously, voluntarily, or under mandate of law, a blood test can be taken. The place of smears, cultures, special tests like the Frei, search for Donovan bodies in biopsies, spinal fluid examination—these may be silver, but they are not gold.

On the morning of the day I wrote these lines, I asked a class of eight public health nurses training as experts in the venereal disease nursing field what they considered the weakest spot in venereal disease control in their 3 months' observation of the problem in university clinics and in public health clinics in a large and, so far as venereal disease is concerned, a highly organized city. "Doctors don't take time to get the history and to make an examination of the patient," said they, and I listened respectfully, for they were contact-tracing and case-uncovering and follow-up experts. I could not help recalling the comment of one of our greatest internists, a Middle Westerner, who said, "The doctor does not examine," and of one of our sagest medical figures in the East, who said, "The doctor does not read."

Two weeks and two days before the incident I have described, 18 men stood around a stretcher on which lay an unclothed patient covered with a blanket. Many of these men had already met diplomate qualifications, and all expected to be dermatologists and syphilologists. They were invited to inspect the patient

preparatory to a discussion of diagnos and treatment: The staphylodermic e zematoid lesions of legs, arms, and true were inspected. A third of the men ha already started back to their seats, who I exclaimed, "Now I have you!" The diagnostic day was saved by three me who plucked at the blanket before I spok and exposed the penis, on which was coronary primary lesion made visible three sutures for experimental biopsy.

Five days before I heard the verdict the nurses, another man lay strippe upon a stretcher. On his penis too wa a biopsied papule. A diagnosis of gran loma inguinale had been made. He wa known to have had a chancre and seco daries, treated 4 months before with 200,000 units of procaine penicillin on a week for 4 weeks (an experimental sy tem). His lesions had cleared, so the story went, and then the induration has appeared on the penis and had been b opsied. The darkfield examination w said to be negative. His titered serolog test for syphilis had taken a sudden le upward after an initial fall, but this t was overlooked. But what was ove looked most of all was a cluster of ring lesions about his chin and nares and half dozen classical secondary recurre papules on the dorsum of his tongue, wi several mucosal mucous patches. If tl man had been seen by your grandfathe and mine-with a keen appraising look finger to the pulse, and a "Stick yo tongue out, my lad!" he would have be diagnosed on sight. No biopsies for gra uloma inguinale for him. Yet this patie had been seen by experts in training he had been seen but not observed, as a chief used to say.

I owe a lifetime's professional debt the country doctor who diagnosed the ficase of acute labyrinthitis in syphilis tl I saw. How did he do it? The man l retching on a bed, the room turning abound. My senior picked up a limp a and pushed the sleeve to the should then out of the corner of his mouth sa "Look!" and I saw the first grouped flicular syphilid, without the slightest in what it was, of my career. But my senithe country doctor, knew what it was.

Failure to examine, inability to spot and integrate evidence, a low index of suspicion, are the obstacles on which the epidemiologic control not only of syphilis but of all yenereal diseases stubs its toe.

Of course, I came to the defense of the profession when the nurses assailed us, and pointed out to them the many reasons why the doctor does not do stripped examinations—the space requirements,

the time requirements, the waiting room full of patients, the telephone, the paper work. Then I had to admit that it takes only a 2- by 2-foot space and less than 7 minutes of time (that's a lot, I know) to do a reasonably thorough examination of a male for a venereal disease. Figure 4 outlines what can reasonably be expected of a physician examining a patient for venereal disease.

Figure 4.—Let's be realistic! What can the practicing doctor do?

We Can Expect:

- .1. The doctor to ask questions. What's the matter? How long have you had it? What have you done about it? Where do you think you got it? Who have you been with?
- 2. A suspiciously alert and intent inspection of the scalp and skin, anus and genitalia, palms and soles, mouth and teeth, lymph nodes.
- 3. A darkfield examination once in a hundred to a thousand times.
- 4. A smear on every male urethral discharge, as a check.
- 5. Cultures for gonococcus, but only at clinical centers, houses of detention, etc.
- 6. Use of serologic tests for syphilis, safeguarded by State approval of laboratories.
- · 7. A serologic test for syphilis on every genital lesion and every exposed person.
- 8. A serologic test for syphilis premaritally and prenatally, every time.
- 9. A serologic test for syphilis before transfusion, operation, and in general medical examination.
 - 10. A simplified form of reporting.
- 11. Knowledge and use of public health resources (diagnostic).
- 12. A growing demand for free antibiotics.

We Cannot Expect:

- 1. Much personal effort at contact tracing, or any great inclination to call State help on it.
- 2. As good an examination of women as of men.
- 3. Routine darkfield examination on primary or secondary lesions, direct or by mail.
- 4. Adequate examination of women once in a hundred times.
- 5. Smear or culture reports before instituting treatment. The doctor must do something *now*.
- 6. Trustworthy serology from uncontrolled laboratories.
- 7. An adequate diagnosis of seronegative primary syphilis.
- 8. Routine blood tests on all patients by any considerable body of physicians.
- 9. Adequate interpretation of the nonspecific or "biologic false" positive.
- 10. Complicated paper work and cpidemiologic questionnaires.
- 11. Much turning over of venereal disease to public facilities.
- 12. Much interest in technically exacting pretreatment diagnosis.

Contact Tracing and the History

This new-fangled business of chasing down the spreaders of venereal disease is the essence of modern epidemiologic control. It ranks with the principle of sterilization of infectiousness by treatment. It is the "from whom, to whom?" question. It is a costly but an indispensable necessity. It requires office work and a field force, exploration of the patient's mind, and exploration and detailed detective knowledge of his world. A trained questioner is not enough. Good contact tracing requires a personality, a photographic and cataloging mind, knowledge of the lingo and the locus, an uncanny ability to put things together, a sort of crossword- or jigsaw-puzzle mind-and footwork, everlasting footwork. Contact tracers who have broken records in numbers of contacts brought in have turned up out of anywhere, in any walk of life; been picked out of the waiting queues in clinics and from the touts and barflies along the waterfront. A good one, well grounded in public health, in the maplike liaison knowledge of his terrain, in sympathy, tolerance, and magnetism, possessed of the come-hither eye and voice, is a priceless asset. Such people are born rather than made. Can the everyday doctor be a contact-tracing asset? Such qualities are rare, even in chiefs of clinics, we must admit. But the doctor can do more than he thinks he can, even if he never moves outside the five questions in figure 4. In the answer to the question, "What's the matter?" one places and esti-"How long?" and mates the patient. "What did you do?" give you a base-line estimate of your public authorities—their success in education, for one thing. took the first World War to increase by one-half of 1 percent the proportion of early syphilis that came in before the second week of the chancre. "Where do you think you got it?" and "Who have you been with?" the doctor ought to askbut the phone rings or his tongue sticks, and he doesn't.

There is a world of human interest and sense of accomplishment open to the doctor who will take the trouble. Especially should he meet the responsibility in the protection of the marital partner, the juvenile and bobby-soxer, the unraveling of the school epidemic, the supplying of the health authority with information on prostitute foci, and the identification of flagrantly promiscuous patients. But realistically, we don't do it, and we are more than slow in calling a nurse or worker into the inquiry.

The worst ailment of contact-tracing effort is common to all attack methods in venereal disease. It is delay. One of my best nurses told me that she would wait for a positive diagnosis of the principal or source before proceeding to seek and bring in the contacts. It took a salvo of argument to make her see the delay involved. Not only does one seem to lose one's time sense, but one tends to become chair-borne in the contact tracer's headquarters. A letter takes the place of a hand on the shoulder. "He says he got it from the girl who jerks soda 2 blocks down at L---'s Drug. Would you go after her?" "Why, u-h-h-h---?"

fe

29

sh

The belief that once a venereal germ enters the human system, sexual relations come to a stop instead of beling stlmulated, and our forgetfulness of the tlcking of the clock, block effective venereal disease control. Add the fact that venereal disease in women is undetected if not undetectable in its infectious stages, and we have a triumvirate of realities against which the gods themselves may fight in vain.

"But hold on a minute, Doctor," you say, "you're getting too realistic! We'll tighten up our examinations, but you say 'What's the use?' We'll ask the hateful questions-yes, we'll allow sitting space in our offices for venereal disease, since a nurse can get the patient out in 'ampule time' and everyone is getting penicillin now for everything anyway, and we won't even have to see him after the first round. We'll even hunt for our pad of blanks and fill out that epidemiologic quiz on your report card and then hunt for the envelope and perhaps the stamp to send it off. And then you tell us it's no use! There's no means of making a darkfield examination in this town, so we'll send

him to the next town with delay (if he arrives at all) and with the possibility of renewed exposure (notwithstanding our warning him not to). The long-distance darkfield by mail, may we say parenthetically, just isn't used. What's left to us, at your service? Why the blood test, of course! And now you're going to tell us that crutch is of no use, either."

Some Limitations of the Smear and Blood Test Approach

The smear involves delay, undependability (especially in women), difficulty in obtaining (especially in women). Culture is feasible, but again there is delay, and the laboratory plant and transmission stymies are serious and expensive. Waiting for these reports in the present status of gonorrhea in the antibiotic age is hard to justify. Smears and cultures become matters for confirmation and record and are hotly disputed as to their meaning for cure. There are fewer and fewer smears, less and less culture likely, except in medicolegal work.

Now as to the blood test for syphilis. You are all aware that it involves delay. A Friday blood arrival at the laboratory may get you no answer before next Wednesday. If it is returned negative, shall you go ahead and treat the genital lesion as a seronegative primary or not? The "golden opportunity," as Pusey called it, is the seronegative primary stage-if you know it's a primary. In fact, the work of Eagle in experimental syphilis indicates that the amount of penicillin necessary to cure syphilis in the incubation period is only one-fourth the amount necessary when the primary lesion appears. And the seronegative, primary-stage human infection is cured by penicillin with only a 1.7- to 4-percent failure rate as compared with 7 to 10 percent for the seropositive and 15 to 30 percent for the full-blown secondary stage. What excuse is there, then, for the serodiagnosis of early syphilis except as a confirmation of a suspicion that it might have been more realistic public health, if not idealistic medical scholarship, to accept the probability as a fact and treat accordingly?

"Now, Doctor, you are back in the salvarsan days, those polemics between Taege and Riecke, which you used to translate so laboriously from German into English. Shall chancroid be treated as primary syphilis?"

Let us further consider the serologic Its performance is open to all comers, more's the pity. But central or pilot laboratory control has gradually become a reality. In Pennsylvania, when in the process of revising the venereal disease control basic law, we made the premarital and prenatal tests compulsory, we made them the basis for a laboratory approval system by insisting that a test which is made compulsory by the State cannot be performed except in a laboratory whose methods, as evidenced by results, conform to a standard, and are periodically checked for conformity to that standard. But the serologist is still too often a prima donna singing his pet stanza in a vacuum. Only recently have some of the larger laboratories accepted conformity. Before we could undertake in serious fashion the study of the biologic false or nonspecific positive reaction in a large blood donor center, it was necessary to tune, as for an orchestra performance, the technics of three participating private laboratories before the clinical and final laboratory group evaluations could begin. The conformity of State with national standards in the United States has had its uphill struggle, too, but is now established.

Well before one gets to the problem of the nonspecific positive, then, one has to realize that uncontrolled serology is seriously untrustworthy and capable wrecking lives, hopes, and happiness. One has to realize that a valuable antigenic discovery like the cardiolipins may lose its specificity in this or that man's private system. One must realize that quantitation (the return of results in units of reagin that fit into accurate curves of therapeutic response) is a modern necessity in testing the blood in early syphilis, in testing the spinal fluid in neurosyphilis, and in testing the blood of the infant of a syphilitic mother. port in pluses now marks reporter and user as "back numbers." Perhaps you would like to see the laboratory report of a patient with neurosyphilis, turned out by a tuned and smoothly running serologic machine (fig. 5), with the jolt thrown into it by a single day of antigen trouble under a technical transition in laboratory control. And while you view

the smooth part of this chart, let me say that the examination of the spinal fluid is so full of crotchets and possibilities of error that hardly one laboratory in five can have its results used interchangeably with those of a standard or top-notch performer.

For several years, the nonspecific posi-

Figure 5.—An example of an accurate serologic record of a patient with neurosyphilis, marred at the end by a false-positive spinal fluid Wassermann, due

to a technical error in the laboratory										
Tabopa Previo Routin	aresis. us treatn le STS pe	nent: 3	30 arsp 1942.	henamir Positiv	ne, 50 l e CSF	ry 7, 1944 bismuth. , Jan. 3, 1 exes O. K.	944. Anisocoria, coarse tremor of			
Date	Days postpeni- eillin	Kline	Cells	Wasser- mann	Pro- tein	Mastic	Clinical			
1944 Jan, 3	Prepeni- eillin	*****	1 ,	0122	2+	1233310000				
,		(1) 1	,200,000 1	units penie	eillin (ev	ery 3 hours)	February 7–11, 1944			
1944 Feb. 7 Feb. 23 Mar. 29. May 3 Oct. 3 1945 Jan. 30	1 18 45 80 233	$ \begin{array}{c} $	5 RBC 4	4444 0122 0124 0012	20 20 20 2012	2444111000 1221000000 2443210000 2221100000 2221100000	Tremor of tongue and anisocoria; otherwise negative. Slight ataxia; impression: no change.			
			(2)	2,400,000 (every 3 l	hours) May 4	H-11, 1945			
1945 May 4 May 8 June 12 Nov. 5	447 451 486 636	21±0 32 Neg.	3 3	0012 0000 0000	20 10 20	2221100000 0000000000 1110000000	Somewhat unstable; has roaring in head. Continues to have roaring in head. Romberg slightly positive.			
1946 Feb. 27	750	21±0	3	0000	20	1110000000	Has had some hallucinations. Impression: paresis worse.			
			(3) 6,40	0,000 (ever	y 3 hour	rs) March 29-	April 8, 1946			
1946 Mar. 29_ Apr. 3	781 786	32	4	0000	20	1110000000				

¹⁹⁴⁷ Jan. 22__ 1,085 Neg. 3 0012 1222100000 Some pain in right ealf; still has roaring in 20 head. Sept. 3... 1,304 4 4 1244 20 2344210000 No change (?). 1948 Neg. Feb. 25. 1,479 0000 20 0000000000 No clinical change.

Dec. 15.. 1,772 Pos.4+ 20 False-positive day in laboratory traced to defective complement. 1110000000

An example of what one false-positive laboratory test may do in the interpretation of the patient's progress on the basis of laboratory reports.

tive test has given medical practice much concern. The concern has not yet caught up with mass blood testing and the "Wassermann barbecue." State, regional, racial and national, industrial, city school, and lodge checks take no account of the inescapable fact (based on several studies, including the results of separation tests in the armed forces) that as high as 40 percent of positives in a common run, especially of a single precipitation test, may be nonsyphilitic positives. As case uncovering by blood testing has stepped up its pace in the past half decade, the consultant's office has been jammed with shocked and bewildered people who, walking in supposed security, found themselves confronted by a positive blood test report. The question, "What does this mean and what to do?" heard at the start from the perplexed and sometimes angry doctor, has changed, and the change is significant of the antibiotic age in syphilis epidemiology. The question now reads, "This woman had a positive, was given 6 million units of penicillin, her baby has had 3.6 million units, both are blood negative, what to do next?" The only answer to that is too often, "Heaven knows!" Again, treatment on suspicion is overtaking diagnosis.

Perhaps it may be bringing coals to Vancouver-Newcastle, but it would round out this part of the text to summarize from one of my previous papers the elementary controls the doctor can place upon the biologic false or nonsyphilitic factor in his diagnosis by blood test. Note that the titered or quantitative test is essential to such differentiations.

- 6. A nonspecific positive is to be suspected under the following circumstances:
- a. If there is complete disagreement between the results of complement fixation and precipitation tests, and especially if it is the precipitation test that is positive.
- b. If the reactions in quantitative tests are fluctuant and of low titer on repetition.
- c. If there exists, or there is a history of an acute infection within thirty days of the time the test is taken.
- d. If repeated quantitative tests (in the absence, of course, of supportive evidence

of syphilis) show over a period varying from ten to one hundred and twenty days a decline to, or close to, negative.

e. In using a precipitation test alone, no matter which one, without a complement fixation check.

f. In winter, as distinguished from summer, testing (respiratory infection season).

7. j. The drawing of blood for a serologic test should be accompanied by *questions*:

(1) Have you had or been treated for syphilis or gonorrhea? Ask again and again.

(2) Have you had malaria?

- (3) Have you had within a month a fever, cold, grippe, pneumonia, or severe sore throat?
- (4) Have you had any preventive inoculations within three months (tetanus, typhoid, smallpox vaccination)?

(5) Have you had blood tests before?

Results?

k. At least a once-over physical inspection.

(1) Pupils.

(2) Rashes (semistripped or stripped).

(3) Oral mucosa and teeth.

(4) Genitalia if possible or indicated.

(5) Tibiae.

(6) Signs of intercurrent infection.1. Temperature, pulse, respiration.

1. Temperature, pulse, respiration. Auscultation of heart and lungs if above normal.

Such basic information and often much more must be regarded as essential to the diagnosis of syphilis by the positive serologic test.³

What is being done to meet the non-specific-positive problem in the blood-test diagnosis of syphilis? It must be admitted, as the old square-rigger sailors used to say, we are hanging in stays. Verification tests have not worked out. The Neurath euglobulin inhibition test is still under investigation and will have a margin of error, I should guess, of not less than 20 percent. It is too complex for mass application, though its extension as a special aid is justified. The best available plan seems to be a clinical or consultant evaluation center that can combine multiple tests from different laboratories

³ Reproduced from pp. 719-20, "Recent Advances in Syphilologic Diagnosis and Treatment. The Nonspecific Positive Serologic Test and the Use of Penicillin," by John H. Stokes, M. D. *The Pennsylvania Medical Journal*, April 1947.

(producing the so-called serologic pattern of the case) with an adequate clinical judgment of examination findings. is a ponderous and expensive mechanism of which the doctor and his patient are understandably slow to take advantage even when it is accessible. What actually seems to be happening is again this transition from pretreatment diagnosis to prediagnostic treatment or treatment on sus-Doctor or patient rightly or wrongly seems to feel that 10 million units of penicillin is as prompt, cheap, and dependable an answer in the doubtful case as the equivocations of a consultant who ends, after expensive deliberations, with inevitable hedging and a recommendation of the same 10 million units of penicillin "just in case" someone should be wrong.

The latest meeting, held in Washington on April 7 and 8, rated cardiolipin-lecithin antigens (there are two), which Arnold and Mahoney (1) say must be standardized for treated and nontreated cases, for climate, for other diseases, and for the detection of nonspecific positives, as the best existing answer. Kline, in discussing their paper, went so far as to say that biologic false-positives are all technical and due to poor antigen. But the Great White Hope of serologic testing is now asserted to lie in a wholly different direction: the detection of Nelson's treponemeimmobilizing antibody in syphilitic serum (2), whose specificity eliminates biologic false positiveness entirely, and whose general application to the serologic identification of syphilis on a large scale awaits only the stymie (which it must be admitted is serious) of the cultivation of virulent Treponema pallidum, whose only available source at present is syphilitic rabbit testicular emulsion.

This series of rather critical, not to say sour, comments on the blood test uncovering mechanism cannot be allowed to pass without a final general endorsement of the STS, the serologic test for syphilis. Nothing at the present time remotely suggests a justification for failure to use it anywhere and everywhere that it can be used, with and without symptomatic prov-

Tragedy lurks behind every ocation. omission, a tragedy so much more serious than the occasional puzzles of false or nonspecific returns, that there is no comparison. A single instance, almost up to the minute, comes from an area in which the law, the practice, and the physician cooperation are all at a high level. graham, Rose, and Beerman (3), surveying a series of cases collected between 1946 and 1948, found 75 pregnant women whose syphilis had been neither recognized nor treated before or during the pregnancy, with a wholesale infant mortality and morbidity (70 percent) that could have been avoided if prenatal care and prenatal blood testing had been carried out. Moore (4) has well emphasized how often the doctor's own family can be involved in an unrecognized syphilis, under the delusion that the profession is sacrosanct and safe.

Is Treatment on Suspicion the Answer?

Before we face this question even more directly than we have up to this point, let us examine a few more straws for wind direction. Certain advances made possible by the antibiotics are essential parts of the problem. The oldest in point of time is the recognition of the importance of what would be adequate treatfor gonorrhea but indubitably insufficient treatment for a masked onset The 600,000-unit level is of syphilis. below the lowest recognized total dose for the treatment of seronegative primary syphilis, and only a tenth of the current standardized total dose for early syphilis recommended to our armed forces by the National Research Council's Subcommittee on Venereal Diseases. It is a little difficult to picture as practicable for gonorrhea a 6-million-unit dose of penicillin, even at a daily single-injection level of 1.2 million units for 5 days. It must be recalled too that prolongation of effect by sustained blood levels is essential to the cure of syphilis in animals. Here the absorption retarders come to our aid. Wright, Nicholson, Arnold, and Mahoney (5) have just reported that a sustained

significant level for 72 hours from a single injection in man is as effective when procaine penicillin in oil with aluminum monostearate is used as was a 7-day round-the-clock course of water-soluble penicillin with the earlier preparations. Combining their views with those of Thomas, Rein, and Kitchen (6) and calling into the estimation Eagle's statement (7) that the sterilizing dose for syphilis in the incubation period is one-fourth the curative dose required when the primary lesion develops, we are practically at the point where a single-dose cure of around 1.5 million units is at hand for syphilis in the incubation period, and for gonorrhea, and, by implication, for effective treatment prophylaxis. It will not surprise you to know that oral penicillin too is under study now as a prophylactic against gonorrhea and that a 300,000-unit tablet will be or actually is available, which will almost certainly be tried in syphilis, notwithstanding that we know next to nothing of its effectiveness except that oral administration with the booster-dose system can maintain adequate blood levels in most patients but that unaccountably some patients fail to show significant blood levels at all. For a number of reasons, the Journal of the American Medical Association recently warned editorially against the trial of oral penicillin as a venereal prophylactic under civilian conditions.

From the attempt to treat syphilis effectively when combined with gonorrhea, and to develop a single-dose cure for both diseases, it is but a step to an attempted single-dose protection from infection of exposed individual. Historically, treatment prophylaxis has been attempted with the arsenicals and with bismuth, but the practice has been confined to the positively exposed single individual. Now Alexander, Schoch, and Mantooth (8), amid protesting Oh-h-h's, have again taken the bull of ping-pong reinfection and contact protection boldly by the horns and reported a 1-day treatment for contacts, consisting of a single 900,000-unit dose of penicillin in oil and wax, a single injection of 60 mg. of mapharsen, and a single injection of bismuth camphocar-They estimated the level of boxylate. infection incidence in untreated contacts at 62 percent, of their treated contacts at 11 percent. This is a maximum figure which they believe is practically negated by the probability that all the failures were reinfections. Last month they reported further studies, omitting the mapharsen injection and using the "system," which they speak of as abortive treatment, in the treatment of symptomatic early syphilis. The results thus far, they believe, compare favorably with generally accepted present-day treatment standards. At the Washington meeting, Plotke and his co-workers (9) reported from the Chicago Rapid Treatment Center, using only 600,000 units as the protective dose, that six times as many infections (25.4 percent) developed among untreated contact controls as among the treated contacts (4 percent) of persons with infectious syphilitic lesions.

I believe we may say that there is developing, then, a rational, practical simultaneous treatment of gonorrhea and syphilis in the incubation period, which can also be applied both to manifest infections and to contacts on suspicion. is true that such a statement must be qualified, as must all penicillin statistics. by the fact that not enough time has elapsed yet for final judgment of penicillin cure. It is even a temptation to imagine the administration simultaneously with procaine penicillin and aluminum monostearate of dihydrostreptomycin, aureomycin (which, as you know, is a rather slow orally administered antisyphilitic), and chloromycetin with aureomycin is active against granuloma inguinale) to all early symptomatic venereal disease and to all persons suspected of exposure, as a massive control effort with possibilities.

Standing on this threshold, then, let us review the field and roughly draft exploratory rules for treatment on suspicion (without positive diagnosis, or on a history of exposure, or on preponderance rather than conclusiveness of evidence) (fig. 6).

Figure 6.—An exploration of principles for treatment on suspicion in venereal disease

- 1. The fields involved:
- (a) Purulent urethritis, vaginitis, and Bartholinitis before smear or culture report is received.
- (b) All suspicious genital lesions, suspicion to include all sexual exposure whatsoever.
- (c) All accessible sexual contacts of a person with infectious lesions, who on explanation can be induced to accept a single-dose or multiple-dose abortive treatment.
- (d) Persons in whom the clinical and serologic evidence for infection is strong but not conclusive.
- (e) Pregnant women with positive blood serologic tests who have not had adequate penicillin therapy for syphilis previously, regardless of the stage or age of their infections.
- (f) Women of promiscuous habits, who may be assumed to have been exposed to gonorrhea, activity not demonstrable because of the difficulty of positive diagnosis.
- 2. The institution of treatment shall be accepted as tantamount to a positive diagnosis, and treatment shall be conducted as if a diagnosis had been made.
- 3. All possible steps to establish a diagnosis of record shall be taken before treatment, e. g., smears, darkfield examination, blood test.
- 4. The treatment shall be the maximum currently accepted for the conditions suspected. Suggestions:
- (a) For early gonorrhea (first week), 1.2 million units procaine penicillin with aluminum monostearate, 600,000 units on first and fourth days.
- (b) For gonorrhea of 2 weeks' standing, 2.4 million units at 600,000 units on first, third, fifth, and seventh days.
- (c) For a suspicious genital (or extragenital) early syphilitic lesion (even though darkfield-negative and seronegative), 6 million units procaine penicillin with aluminum monostearate, 600,000 units daily or every other day, or 6 days a week.
- (d) For venereal contacts, including suspected incubation stage syphilis, 1.2 million units procaine penicillin with aluminum monostearate; 600,000 units in each buttock or 600,000 units a. m. and p. m., same day.
- (e) For pregnant syphilitic women, early or late infections, and pregnant women exposed to syphilis, 4.8 million units at 600,000 units daily of procaine penicillin with aluminum monostearate.
- (f) For probable biologic false positives (nonspecific positive reactors), especially pregnant women, 4.8 to 6 million units.
- 5. A separate category in reporting shall be provided by the health authority for treatment on suspicion.
- 6. The follow-up and cure criteria shall be adhered to as rigidly for the suspected as for the demonstrated infection (this to include a quarterly check for 2 years on all suspected incubation or clinical early syphilis, and a year on gonorrhea).

These are suggestions for your consideration, not rules for your observance.

For one who came to this occasion resolved only to present perspective, not to advocate decision, you will see that, like the turtle, I have rather stuck out my neck as I walked. Those of you who are concerned with medicine as an intellectual discipline, and differential diagnosis as one of its choicest expressions, will shudder at the ultimates suggested by such an approach to the epidemiology of the venereal infections. That this radical and heterodox procedure is capable of extinguishing venereal disease, even with the advances which one can already envisage for the near future, seems to me improbable. But far more improbable in fact, quite impossible—appears to me the extinguishing of pretreatment-diagnosed venereal disease. Short of the hoped for but still remote achievement of immunization, prerecognition and suspicion therapy, even with its chances of relapse, its margin of untraced contacts, its battledore and shuttlecock reinfections, seems, in the new age, definitely the better bet.

The Problem of Promiscuity

I have deferred to a closing paragraph a mere mention of a critical topic, which I have presented more fully elsewhere. Cold analysis of the accomplishments of the chemotherapeutic age in the control of venereal disease, aided by all the contributory efforts that a generous government has put at the disposal of venereal disease control workers, has not been too encouraging. Ground gained at one point has been lost at another. The reinfection problem in syphilis, the weekly gonorrhea, the spread of venereal disease downward into teen-age and childhood, the reappearance of sinister trends like wide-open prostitution and sex commercialization, prophylaxis without regard for social and moral implications, the imperiled status of the family, are only a few of the salients at which critical battles are being fought on a front that embraces all of human life. Mere treatment of venereal disease is certainly not the answer. And were it the answer, and were venereal diseases wiped out, it is

now clear that the accomplishment would have heavy costs in the social, moral, and material life of man. A world of accepted, universalized, safeguarded promiscuity is something to look at searchingly before it is accepted. Venereal disease is now seen as flag-bearer for a social ailment, a maladjustment, shall we say, an unbiologic and asocial trend in the behavior of man. If promiscuity is not to be accepted, and I say for myself, unhesitatingly, it should not be, a whole new arsenal of weapons must be brought to bear upon the sex and venereal disease problem. It is a reasonable question, whether by eliminating disease, without commensurate attention to the development of human idealism, self-control, and responsibility in the sexual life, we are not bringing mankind to its fall instead of its fulfillment. When, as he sometimes does, the physician takes the stand that his business is the extinction of disease by any and every method, regardless of its moral repercussions, and lets the chaplain look after the rest, he is on dangerous ground. First of all, he is a leader of men, and secondly, a servant of bodily health. If he debases the spirit of man by the methods he employs to save his body, he is indeed the Devil's servant. If he is to measure up to his humanistic tradition he must concern himself constructively with the conservation of family living, and with education for it.

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The Health Department and Private Physician Team in Venereal Disease Control¹

W. Elwyn Turner, M. D., M. P. H.

Introduction

Although much study has been devoted to the means by which health departments can develop and improve their methods of venereal disease control, too frequently the role of the private practitioner in control programs has been minimized or disregarded entirely.

A health department may, in a given area, do everything possible to control venereal disease: it may have an excellent clinic operating full time at convenient hours; it may have, in addition to a well-trained venereal disease control officer, capable and well-trained nurses, investigators, and clerks, all unexcelled in epidemiologic skill and effort; and the results of its treatment and follow-up may be completely satisfactory. With such a program, the incidence rate of venereal disease may be reduced to a certain level;

but, in order to reduce this rate further, something more than control by the health department is necessary—the cooperation of the private physician. This is especially true in the control of the venereal diseases.

It is a well-known fact that a large majority of venereal disease cases are seen by the private practitioner; also well known is the fact that little or nothing is done in the way of epidemiology in most of these cases. Yet epidemiologic study and contact tracing are as essential in cases diagnosed in the private office as in cases diagnosed in public clinics. The practicing physician who has confidence in and who fully cooperates with the health department can aid greatly in further lowering the venereal disease incidence rate.

To demonstrate the necessity of cooperation between private physician and health department, a special project was conducted in Santa Clara County, Calif., during 1948.

¹ From the Santa Clara County (Calif.) Health Department.

Description of Project

Santa Clara County, located just south of San Francisco Bay, covers an area of 1,312 square miles. Of a total population estimated at 269,400 in 1948, 123,876 are classed as rural. San Jose and Palo Alto, the largest of 9 incorporated cities, had populations of 84,826 and 23,648, respectively, in 1948. The population of the county, predominately white (approximately 2 percent oriental and 1 percent Negro), is agricultural and stable, with the exception of an influx of about 20,000 seasonal migratory agricultural laborers in summer months.

Santa Clara County is served by two full-time health departments—the San Jose City and the Santa Clara County cooperation Departments. In Health with the United States Public Health Service and the California State Health Department and cosponsored by the Santa Clara County Medical Society, the health departments of Santa Clara County jointly have conducted a venereal disease project to demonstrate: (1) that the private physician, with the full support of local health agencies, can perform the essentials of venereal disease control, including case finding, diagnosis, treatment, contact interviewing, and posttreatment observation; and (2) that a public education program, featuring symptoms and speed of treatment and emphasizing the private physician as a public servant, can accelerate case finding for both the private physician and the local health department.

Since certain aspects of the Santa Clara County program were planned to become permanent, it was therefore essential that preliminary work be done on a sound To this end, a careful development of interest on the part of the private physians of the county was started. The "Physicians Bulletin," a monthly publication of the Santa Clara County Health Department, carried a series of articles on various aspects of venereal disease control, including diagnosis, treatment, details of reporting, and contact interviewing. An article explaining the project was published in the medical society bulletin, and a regular meeting of the medical society was devoted to a talk by Dr. E. Gurney Clark on the modern treatment of syphilis. A series of 12 staff in-service training lectures for public health nurses was given; these were generalized in order to make the project not only a demonstration but also a permauent part of the venereal disease control program, and to integrate it into the total health program. Numerous staff meetings were also held to orient the district public health nurses, who called on nearly all the physicians in the county, explaining the program and pointing out the services furnished by the health departmentconsultatiou, diagnostic procedures, epidemiologic investigation, drugs (including penicillin), and nursing service. Doctors were encouraged to report their cases and to utilize the services and facilities of the health department staff whenever advisable; return visits were made to their offices by request or on follow-up of reported cases. Physicians in the county were almost unanimous in their approval of the program.

During the remainder of the project, an educational program was conducted eiuploying a variety of mediums, including radio, newspaper, signs in public lavatories, match-book advertising, movies, comic books, film strips, lectures, and These pamphlets. materials, which stressed venereal disease signs and symptoms and ease of cure, directed suspects to their doctor or health department.

A new venereal disease comic book in color, "Kid Pancho," was developed on this project. The story of Kid Pancho was also put on a film strip, with a recording, and on 16-mm, colored film with sound In the latter form, this story proved very useful on the "Adsovision," a new device which projects up to 25 minutes of film over and over indefinitely, without rewinding or stopping. venereal disease subjects, interspersed with sports or comic shorts, were very effective on the Adsovision and attracted much attention at a busy bus terminal where they ran continuously for about 10 hours daily over a period of 6 weeks. A time-clock device automatically starts and stops the show as desired.

Results of Project

As a result of this project, physicians and the general public showed increased interest in venereal disease. For instance, 63 physicians made special request for venereal disease pamphlets to distribute to their patients. Several physicians stated that patients were coming to their offices requesting blood tests and venereal disease examinations. A great increase in clinic prediagnostic work was also seen. During the period of the project, the number of blood tests done by private physicians totaled 38,528, an increase of 13,133 over the 25,395 blood tests done by private physicians in 1947.

Since the incidence rate of venereal disease in Santa Clara County is relatively low, any attempt to evaluate statistically the effectiveness of private physician participation and the public educational program yields unspectacular results. The following points, however, indicate that the project has had some measure of success.

Syphilis reporting, Santa Clara County	1947	1 948
Private physicians re-		
porting cases	71	112
Syphilis cases reported		
by private physicians	140	254
Contacts to syphilis cases		
reported by private		
physicians	0	141

Comment

This project has been very successful in increasing the confidence of the private practitioner in the health department and in making the health department staff more cognizant of the problems of the private practitioner.

Doctors, having been made aware of the services and facilities provided by the health department, have shown their approval of the project by an immediate and great increase in the reporting of not only the venereal diseases but of all communicable diseases and by an increase in requests for information, consultation, services, and drugs. All divisions of the health department noticed an increase in requests soon after the program started.

Santa Clara County has had a fulltime, intensive venereal disease control program since 1937, and incidence rates have remained consistently low; this project, therefore, did not uncover a large number of cases of infectious venereal That the project was of inestimable value, however, worthy of continuation in the county and repetition elsewhere, is evidenced by the rapport built up between the venereal disease clinic and the private physicians treating venereal disease and by the more complete reporting of both contacts and cases. Nurses are being called upon to interview cases for contacts; the clinic is being requested to afford consultations, to check spinal fluids, and to furnish penicillin. That the public is becoming more aware of the importance of venereal disease is shown by the increased number of prediagnostic examinations done at the clinic and by the requesting of venereal disease examinations, including a blood test, by persons seen by private physicians.

Although the main objective of the program, an effective working partnership between the private physician and the health department, cannot be accurately measured statistically, the venereal disease clinic staff estimates that at the present time, a year after the program was started, more than 75 percent of all epidemiologic work in Santa Clara County originates with the private physician.

This project has therefore demonstrated that the health department and the private physician, working together, can accomplish a venereal disease control program which will reduce to a minimum the incidence of new cases.

Darkfield Microscopy: Some Principles and Applications¹

Frank W. Reynolds, M. D., M. P. H., and Edwin N. Hesbacher, M. D., D. P. H.

I. The Technic of Darkfield Microscopy

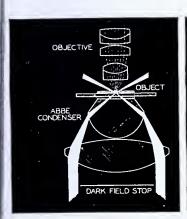
Principle

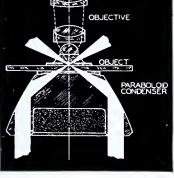
Darkfield illumination consists in blocking out the central rays of light and in directing the peripheral rays from the side upon the microscopic object under study. Under these conditions light does not enter the objective directly, only those rays which are reflected upward by the object passing into the eyepiece. The object thus appears bright against a black back-

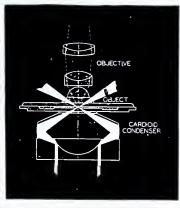
quired to identify the *Treponema pallidum*, a special condenser is necessary.

The Condenser

The darkfield condenser provides means of blocking out the central rays of light directed upward by the mirror. In its simplest form, it is merely an Abbé condenser with a darkfield stop; but the newer paraboloid and cardioid types of condenser are much more satisfactory







Abbé condenser with darkfield stop

Paraboloid condenser

Cardioid condenser

(Bausch & Lomb Optical Co., Rochester, N. Y.)

FIGURE 1.

ground, just as minute dust particles in the atmosphere become visible when a ray of sunlight enters a darkened room.

The Darkfield Microscope

The darkfield microscope differs from other microscopes chiefly in the condenser used. Darkfield illumination for low-power work can be obtained by means of the central-disk ring stops which accompany most microscopes when purchased. However, for the oil-immersion work re-

since they bring more light to bear upon the object. With any of the three (fig. 1), the object under study is illuminated by an annular hollow cone of light, the apex of which is coincident with the object.

It is readily apparent that the condenser must be centered accurately. Indeed, a poorly centered condenser is the most frequent source of error in darkfield microscopy. There are now on the market microscopes with built-in, precentered condensers (fig. 2). For routine clinic work, when darkfield examinations frequently are performed, these are quite satisfactory, although disadvantageous in that the condenser cannot be focused.

¹From the Department of Dermatology and Syphilology, Medical College of Virginia, Richmond, Va.

More often, miscroscopes with interchangeable brightfield and darkfield condensers are used (fig. 3). These must be carefully centered each time a change is effected (fig. 4).

Many condensers have engraved upon their top surface a *eentering circle*, which

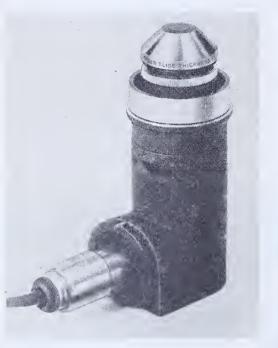


FIGURE 2.—Bausch & Lomb darkfield illuminating unit with precentered bulb and condenser. (Bausch & Lomb Optical Co., Rochester, N. Y.)

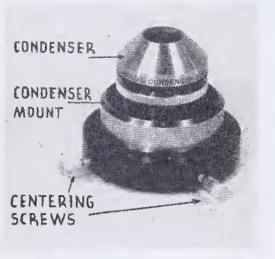


FIGURE 3.—Bausch & Lomb paraboloid darkfield shown removed from substage ring. (Bausch & Lomb Optical Co., Rochester, N. Y.)

may be visualized through the low or high dry objective. If this circle appears directly in the center of the field of vision, the condenser is properly centered. If not, centering can be effected by adjusting the set-screws at the side of the condenser mount (fig. 5). Lacking a centering circle, the condenser may be centered by gradually bringing the apex of the hollow cone of light (seen when the condenser is lowered slightly) directly into the center of the field.

The condenser must also be focused accurately, since the cone of light must converge sharply upon the object being studied. Since slight changes in the height of the condenser materially affect the clarity of the image, a fine adjustment for focusing the condenser is desirable, although not requisite.



FIGURE 4.—Bausch & Lomb darkfield illuminating unit, centering type. (Bausch & Lomb Optical Co., Rochester, N. Y.)

The Objective

Objectives of a high numerical aperture allow entrance of direct rays of light about the margins of the lens and hence are not satisfactory for darkfield work. To be satisfactory, the objective must be of a numerical aperture less than 0.9. Oil-immersion objectives especially designed to be of low aperture can be purchased but are expensive. Objectives of higher

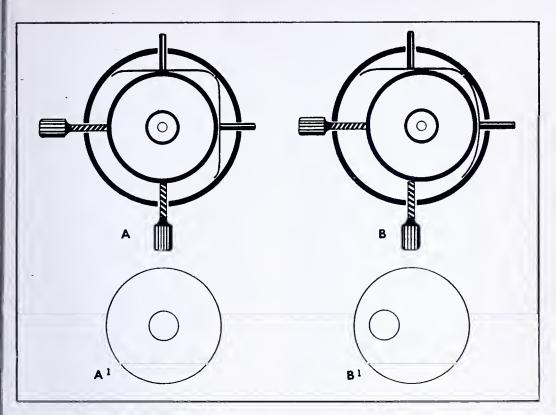


FIGURE 5.—Diagram showing centering arrangements of paraboloid darkfield condenser. A shows centered condition. A¹ shows position of centering circle as seen in microscope field. B shows condenser decentered. B¹ shows field under this condition. (Bausch & Lomb Optical Co., Rochester, N. Y.)

aperture can be utilized if some means of compensating for this factor is provided. Compensation can be effected with either (1) a funnel stop, or (2) an iris diaphragm within the objective.

The funnel stop (fig. 6) is a small hollow metal cone inserted into the objective, which lowers the effective numerical aperture. Funnel stops for one make of objective rarely fit those of other manufacturers. They are cheap and effective but inflexible.

The principle of the *iris diaphragm* is that of the camera shutter. When built into the objective (not the condenser) it provides a flexible adjustment of effective numerical aperture, which allows one to compensate for varying thickness, color, and opacity of the glass slide and coverslip. These objectives are expensive and have the disadvantage of being easily ruined should oil enter the objective about the iris diaphragm.

The Light Source

Since only a small portion of the light reflected upward by the mirror enters the condenser because of the central opaque stop, the source of light must be considerably stronger than that used for ordinary microscopy. It is impossible to use skylight or diffused light from frosted bulbs when working with the darkfield illuminator. A light source of high intensity can be obtained from a bulb with a band filament or, better still, from a carbon arc (those operating on direct current being better than those using alternating current). Condensers fitted with a builtin, precentered lamp have been found entirely satisfactory and are becoming more and more popular.

Object Slide

For darkfield microscopy, the object slide must be of correct thickness, so that the apex of the cone of light coincides with the object being studied. If the

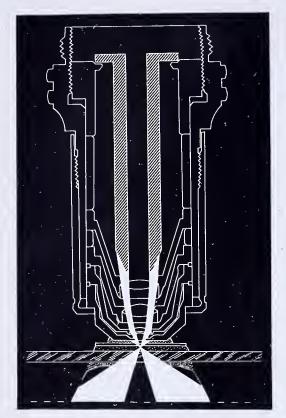


FIGURE 6.—Diagram showing median longitudinal section of 97 × oil-immersion objective with funnel stop in place. Path of light shown from top of darkfield condenser through specimen and objective. Funnel stop prevents direct rays from functioning in image formation. (Bausch & Lomb Optical Co., Rochester, N. Y.)

slide is too thick, this cannot be realized. Thinner slides may be used, although some difficulty may be encountered in maintaining the thicker layer of oil required. The optimum slide thickness usually is marked on the darkfield condenser and should not be exceeded. A slide thickness of 1.3 mm. to 1.5 mm. and a No. 1 coverslip usually make a satisfactory combination. A certain amount of compensation for object slide thick-

ness may be attained by focusing the condenser up or down.

The Preparation

The object slide and coverslip must be scrupulously clean and free from scratch marks. Inclusion of air bubbles in the material under the coverslip is to be avoided. The preparation should be thin in order to avoid excessive flow of liquid passing across the field of vision.

Because the refraction of light must be uniform throughout the condenser-objective system, cedar oil, mineral oil, or glycerin must be placed not only between the objective and the coverslip but also between the condenser and the slide as well.

Common Sources of Error in Darkfield Microscopy

The most frequent reasons for unsatisfactory darkfield preparations are outlined below:

- 1. Improper use of the condenser:
- (a) Failure to center condenser properly.
- (b) Failure to focus condenser accurately.
- 2. Improper use of the objective:
- (a) Use of objective with too high numerical aperture or failure to compensate with either a funnel stop or iris diaphragm.
- 3. Inadequate light source.
- 4. Faulty preparations:
- (a) Excessively thick glass slides or coverslips.
 - (b) Dirty or defective glassware.
- (c) Inclusion of too many refractile objects (R. B. C., air bubbles, tissue cells, etc.).
- (d) Excessive amount of fluid between slide and coverslip.

II. Darkfield Microscopy and Clinical Syphilology

Treponema pallidum is demonstrably present in accessible lesions only during the early stages of syphilis. It is useless to search for them in the late lesions of

the skin or in gummas. In early lesions, however, they are present and usually can be demonstrated by darkfield microscopy.

All too often in the past, the combina-

tion of a genital sore and a positive serologic test for syphilis has been taken as prima facie evidence of the existence of early syphilis. That this is a dangerous practice is apparent to any who consider that (1) nonsyphilitic genital lesions may appear in patients with late syphilis; and (2) nonsyphilitic genital lesions not infrequently (20 to 30 percent) cause transiently positive serologic tests for syphilis in individuals who do not have this disease.

It is essential, therefore, that a search for *T. pallidum* be made whenever there is any suspicion that a given lesion, whether of the genitalia, skin, or mucous membranes may be syphilitic.

Collection of the Specimen

In collecting specimens for examination, care must be taken to protect the examiner from accidental infection. Obvious cuts and abrasions are not necessary to allow entrance of treponemes. The organism is of microscopic size and may enter through microscopic breaks in the skin. Rubber gloves should always be worn.

Exposed genital lesions are readily studied. The surface of the lesion should be cleansed carefully with saline, dried, and then gently abraded to the point of bleeding. Gentle pressure is maintained upon the bleeding points until only clear serum exudes. To increase the exudation of serum, the base of the lesion may be squeezed gently or a suction cup may be applied. A drop of xylol placed upon the lesion to induce local hyperemia will increase the yield of serum. The xylol must be wiped off carefully before the specimen is collected.

The presence of phimosis may make the lesion inaccessible. Usually the phimosis can be reduced by persistent traction following the application of mineral oil. If this fails, a simple dorsal slit through the prepuce may be performed.

Collection of satisfactory material from lesions of the cervix is more difficult. After removal of all cervical discharge, the lesion is cleaned with saline, dried, and abraded as before, usually by rubbing with gauze upon a Kelly clamp. As bleeding stops and serum exudes, material can be obtained by using a long capillary tube equipped with a suction bulb.

From lesions of the skin, material for darkfield examination can be obtained by making multiple small linear incisions with a sharp scalpel or by aspiration of the base of the lesion through a fine hypodermic needle. Moist papules (condylomata) require gentle abrasion only. With macular lesions, some have used the expedient of applying a cantharides patch, which is retained in place 24 hours. Serum in the resultant vesicle may be used for microscopic study. T. pallidum can be demonstrated most readily in papular lesions, and condylomata lata usually teem with organisms. With careful technic, however, treponemes can be fairly easily demonstrated in most skin lesions of secondary syphilis.

In obtaining material from mucous patches in the mouth, particular care must be exercised to avoid contamination with the mouth spirochetes so frequently part of the usual flora. The lesion should be walled off as completely as possible with cotton strips, cleaned, and dried before being abraded.

If local therapy has been used, it will be difficult or even impossible to find treponemes. The use of compresses of boric acid or saline for 24 hours often will facilitate finding the organism. Local therapy should be restricted to these compresses alone.

Aspiration of enlarged lymph nodes is a practicable method of obtaining material for darkfield study, which ordinarily is free from contaminating organisms which are confused with *T. pallidum*. A small hypodermic needle and a 2-cc. syringe are used. It is not necessary to inject solutions into the node. If the syringe is washed out with saline just before use, sufficient fluid will be present. Antiseptic precautions are, of course, necessary.

Identification of Treponema Pallidum

Under the darkfield microscope, *T. pallidum* can be identified by (1) its morphologic characteristics; and (2) the characteristic types of movement.

Morphologically, *T. pallidum* is a delicate spirilliform organism with regularly spaced, tightly wound coils. It varies in length from 5 to 25 microns, usually two to three times the diameter of a red blood cell. Toward the ends, where the body is thinner, the coils may be spaced somewhat more widely. The spiral coils are consistently retained despite active motility.

The characteristic motions are: (1) movement forward and backward; (2) rotation on its own long axis like a corkscrew; and (3) slow undulation. The organism gives the impression of over-all flexibility, as though able to bend its body at any point. Most commonly the bending is at or near the middle. It lacks the rapid lashing movement of other spirochetes and progresses forward or backward so slowly that ordinarily it is not difficult to keep the same specimen within a single microscopic field.

T. pallidum is the gentleman of the spirochete family—he, as Warthin says, "of the waxed moustache." Always maintaining his dignity of coil, never threshing aimlessly about, he proceeds to his destination with a certain savoir-faire which allows time for a gentlemanly bow from the middle.

It should be emphasized that definitive differentiation of *T. pallidum* from other spirochetes depends not only upon the morphologic characteristics but also upon recognition of the typical movements as well. In tissue sections stained by silver impregnation or in dried specimens prepared with India ink, the important differential factor of movement is lost.

Open lesions should be examined repeatedly by darkfield microscopy as long as serum can be obtained for study. In our experience, however, if *T. pallidum* is not demonstrated after three to five preparations have been carefully made, reliance should be placed on other diagnostic criteria rather than upon the darkfield examination. Definitive diagnoses based upon the finding of a single organism after prolonged search are not trustworthy and should be avoided.

Spirochetes With Which T. Pallidum May Be Confused

Because the classification of the genus *Treponema* depends almost exclusively upon poorly defined morphologic characteristics, few clear-cut differentiations within the group are possible. The nomenclature of the organisms within the genus is utterly confused.

One of the most satisfactory criteria for differentiating *T. pallidum* from non-pathogenic spirochetes commonly found in the mouth and upon the genitalia is that when more than one *T. pallidum* are found, the organisms are quite uniform in shape, size, and movement. The saprophytic organisms practically always are mixed, so that any one specimen contains spirochetes of various sizes, shapes, and types of movement.

Mouth Spirochetes

A number of morphologically distinct types of spiral organisms are present in the human mouth, more frequently and more abundantly when oral hygiene is poor. These spirochetes are best differentiated according to size: the smaller forms, Treponema microdentium; the intermediate forms, Treponema macrodentium and Treponema vincenti; and the larger forms, Treponema buccale.

All these spirochetes, except T. micro dentium, have flatter, more irregular, and more widely spaced coils than T. pal flexible and lidum; they are more more actively as well as awkwardly motile. T. microdentium, ordinarily some what shorter and thicker than the treponeme of syphilis, may at times resemble it so closely as to be practically indistinguishable. T. macrodentium and T vincenti are not so troublesome. Both are larger than T. pallidum, but the former is thick of coil whereas the latter is delicate and has irregular, loosely wound spirals T. buccale, a long, thick, double-contoured organism with wide, flat coils should cause no difficulty at all.

Genital Spirochetes

The normal flora of the male and female genitalia includes numerous spirochetes, ordinarily saprophytic, but which in symbiosis with other anaerobic organisms may cause dirty, erosive, and gangrenous lesions. These spirochetes frequently invade and complicate other ulcerative lesions of the genitalia, such as those due to *T. pallidum*.

As with those found in the mouth, the spirochetes found upon the genitalia may be classified according to size: the smaller forms, *Treponema genitalis*; the intermediate forms, *Treponema calligy-rum*; and the larger organisms, *Treponema refringens*.

These treponemes, except *T. genitalis*, differ from *T. pallidum* in that they have wider, flatter, and more irregularly spaced coils and more active, ungainly movements. *T. genitalis*, morphologically almost indistinguishable from *T. microdentium*, most nearly approximates *T. pallidum* in size and appearance but may be somewhat thicker and may have deeper and more widely spaced spirals.

Artefacts Commonly Found in Darkfield Preparations

Specimens under study may contain: erythrocytes with their rouleaux formations; leucocytes, epithelial cells, platelets, and powdery hemokonia. Forms not unlike treponemes result from formation of spiral fibrin filaments. Cilia, flagella, miscellaneous pieces of cellular debris, and fine scratch marks in glassware also may have a deceptive spirochetal appearance. There is considerable Brownian movement of the small particles suspended in all darkfield preparations.

The Delayed Darkfield Examination

To practitioners who do not have facilities for darkfield examination, some rep-

utable laboratories have made available capillary tubes for the collection of specimens which may be mailed to the laboratory for study.

The feasibility of the delayed darkfield is indeed questionable. If the examination can be carried out promptly, before the motility of the spirochetes is lost, the results are valid. More often than not, however, the lapse of time precludes observation of the typical movements of *T. pallidum*, and the diagnosis is then based upon morphologic characteristics alone—a misleading and dangerous practice.

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CURRENT NOTES AND REPORTS

Social Hygiene Day, 1950

February 1, 1950, marks the local community observances of Social Hygiene Day, with the largest meeting scheduled for New York City at the Hotel New Yorker.

These observances are designed to enlist citizen support of social hygiene objectives, which this year stress education to prevent venereal infections, particularly through training of youth through home, church, and school for successful marriage and family life. The slogan for Social Hygiene Day, 1950, is "Social Hygiene is a Family Affair."

Held under the national sponsorship of the American Social Hygiene Association, with the cooperation of the United States Public Health Service, the observances in thousands of cities and towns in the United States and the Territories serve to focus public attention on the need for social hygiene programs and to spark year-round efforts.

All avenues of reaching the public, including newspapers, magazines, radio, and television serve to channel out publicity on the events of the Day, which in many areas are officially proclaimed by governors of States and mayors of cities. To aid in planning these local events, the Association is preparing an attractive, illustrated publication for wide distribution, along with informational materials.

Any communities which have not yet instituted annual observance but which wish to participate in or to launch a social hygiene society, may get suggestions and free materials by writing to the Social Hygiene Day Service, American Social Hygiene Association, 1790 Broadway, New York 19, N. Y.

Western Seminar Papers Now Available

The "Digest of Proceedings" of the Western Venereal Disease Control Seminar, held in Los Angeles on May 29, 1949, is offered for distribution.

Seven of the eight papers presented

have been assembled in a 37-page mime graphed booklet, obtainable on reque from the Regional Director, United State Public Health Service, room 441, Feder Office Building, San Francisco 2, Calif.

International Abstracts on Venereal Diseases Available

Announcement is made by the publishers of *Execrpta Medica* of the availability of section 13, "Dermatology and Venereology." Abstracts are presented in this section that deal with selected articles on physiologic, pharmacologic, endocrinologic, and bacterioserologic subjects relevant to dermatology or venereology.

Excerpta Medica, an international me ical abstract service which is published. English and which covers the whole fie of clinical and experimental medicin can be obtained through the Williams Wilkins Co., Mount Royal and Guilfor Avenues, Baltimore 2, Md.

1949 Symposium Published

Proceedings of the 1949 "Symposium on Current Progress in the Study of Venereal Diseases" have been published. The symposium was held in Washington, D. C., on April 7 and 8, under the auspices of the Syphilis Study Section of the United States Public Health Service, which met in conjunction with the American Venereal Disease Association.

The 1949 Symposium contains 32 papers

by members of the Syphilis Study Section, 11 of which were read by title only. It also contains 23 papers prepared by members of the American Venereal Disease Association, 5 of which were read by title only.

Copies of the 1949 Symposium can be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 75 cents each.

CURRENT LITERATURE

Note: Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 25 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

ACTA MED. ORIENT., TEL-AVIV

Singultus. [Syphilis.] J. Kleeberg. 7: 91-102, May-June 1948; 135-145, July-Aug. 1948.

AM. J. M. Sc. PHILADELPHIA

Rapid attainment of therapeutic penicillin concentrations in the cerebrospinal fluid.
William P. Boger and William W. Wilson. 217: 593-599, June 1949.

Some cardiological problems of the tropics. [Syphilis.] E. Garcia Carillo. 217: 619-626, June 1949.

Prozone phenomenon in the serodiagnosis of syphilis. A clinical study. Virginia P. Beelar, Hyman J. Zimmerman and Benjamin Manchester. 217: 658-665, June 1949.

The treatment of pneumonia and other infections with a soluble sulfonamide, gantrosan (NU-445; 3 4-dimethyl-5-sulfanilamido-isoxazole). [Gonorrhea.] Robert L. Brickhouse, Mark H. Lepper, Thomas E. Stone and Harry F. Dowling. 218: 133-137, Aug. 1949.

The treatment of gonorrheal arthritis with penicillin. Norman Spitzer and Otto Steinbrocker. 218: 138-144, Aug. 1949.

Pernicious anemia complicated by syphilis. Report of three cases. Simon Zivin and George V. LeRoy. 218: 179-185, Aug. 1949.

AM. J. MED., NEW YORK

Dosage forms of penicillin for systemic infections. Chester S. Keefer. Seminars on Antibiotics. 7: 216-220, Aug. 1949.

Recent advances in streptomycin therapy.
Ralph Tompsett and Walsh McDermott.
Seminars on Antibiotics. 7: 371-381,
Sept. 1949.

Effect of aureomycin on the survival of virus in lymphogranulomatous buboes. John W. Runyan, Lisbeth M. Kraft and Irving Gordon. American Federation for Clinical Research. [Abstracts of papers presented at the national meeting held in Atlantic City May 3, 1949.] 7:419–420, Sept. 1949.

AM. J. OBST. & GYNEC., ST. LOUIS

Sickle cell anemia and pregnancy. [Syphilis.] George W. Anderson and Trent Busby. 58: 75-89, July 1949.

AM. J. PSYCHIAT., BALTIMORE

Analysis of mortality and causes of death in a mental hospital. [Syphilis.] Herman Josephy. 106: 185-189, Sept. 1949.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

- *The susceptibility of various strains of mice to experimental syphilis. Harold J. Magnuson, Barbara J. Rosenau and J. W. Clark, Jr. 33: 308-317, July 1949.
- *Observations on the growth of the nonpathogenic Nichols strain of *Treponema palli*dum in the embryonated chick egg under anaerobic conditions. Victor D. Newcomer and Merle Haanes. 33: 318-322, July 1949.
- *Relationship of early clinical failure to serologic response in penicillin-treated early syphilis. Mark T. Hoekenga, Minerva S. Buerk and Rowland V. Rider. 33: 323-333, July 1949.
- Reinfection in syphilis. George E. Peabody and Bruce Webster. 33: 334-356, July 1949.
- *Penicillin treatment of late neurosyphilis—one- to five-year follow-up with special reference to clinical failures. David Landau, Israel Kopp, Augustus S. Rose and Harry C. Solomon. 33: 357–363, July 1949.
- *Difficulties in the evaluation of treatment procedures in tabes dorsalis. Herbert Koteen. 33:364-379, July 1949.
- Describing a contact of venereal disease. Nicholas J. Fiumara. 33: 380-388, July 1949.
- *Aureomycin in the treatment of granuloma inguinale. Raymond C. V. Robinson, Dumont F. Elmendorf, Jr. and Harold E. C. Zheutlin. 33: 389-396, July 1949.

The susceptibility of various strains of mice to experimental syphilis. Harold J. Magnuson, Barbara J. Rosenau and J. W. Clark, Jr. Am. J. Syph., Gonor. & Ven. Dis., 33: 308-317, July 1949.

Nine strains of the laboratory mouse (Mus musculus) were tested for susceptibility to infection with Treponema pallidum (Nichols strain) as measured by the infectiousness of their tissues for the rabbit on intracutaneous inoculation. Experiments were limited to male mice weighing between 15 and 20 gm. at the time of inoculation. The inoculum was an emulsion prepared from acute testicular syphiloma of rabbits inoculated 14 days previously with T. pallidum. Each mouse received 0.2 cc. organisms intraperitoneally. Four weeks after inocula-

tion the mice were killed by exsanguination from the heart, the tissues removed and ground separately with 1 cc. of 50percent normal rabbit serum. The entire cerebrum, spleen, contents of the popliteal fossae (lymph nodes), the gastrocnemius muscles, a lobe of the liver, and the blood from cardiac puncture were the tissues assayed. After thorough grinding, onefifth of each emulsion was inoculated intracutaneously into each of 5 sites on the backs of 5 different rabbits. From 12 to 24 sites were inoculated on each rabbit. Each mouse tissue was thus tested for infectivity at 5 different sites all on different rabbits. The inoculated sites were examined weekly during a 3-month period. Lesions developing at any one of the sites were considered positive only if T. pallidum could be found on darkfield examination.

Twenty mice of each strain were inoculated, but this report is limited to 10 mice of each. The other 10 are being carried for 1 year after inoculation before killing and transfer.

The extreme variation among strains and among mice of the same strain is apparent. Among the nine strains of the same species, there was a wide variation in susceptibility to the infection as measured by the relative infectiousness of the mouse tissues on transfer to rabbits. In none of the nine strains tested did symptomatic infection develop.

In order of decreasing susceptibility the strains were: CFW, CF-1, C₃H, CW, C-57 black, Chocolate, dba-line 1, State Laboratory, and Brown Spot. In order of decreasing infectiousness the tissues were: spleen, liver, brain, blood, lymph node, and skeletal muscle.

Observations on the growth of the non-pathogenic Nichols strain of *Treponema pallidum* in the embryonated chick egg under anaerobic conditions. Victor D. Newcomer and Merle Haanes. Am. J. Syph., Gonor. & Ven. Dis., 33: 318–322, July 1949.

The purpose of this paper is to report the successful cultivation of the nonpathogenic Nichols test tube strain of eggs. On the basis of the survival and multiplication of *T. pallidum* in the dead human fetus, it seemed apparent that viable fetal tissue was not necessary for the growth or survival of the organism, and for that reason, it was decided to attempt growth of *T. pallidum* under anaerobic conditions in killed chick embryos.

Ten-day-old viable chick embryos were used in the experiments. One cubic centimeter of the culture fluid containing the organisms was inoculated into the yolk sac, the chorioallantoic sac, and the chorioallantoic membrane of the embryonated egg. Anaerobic incubation was carried out by placing the inoculated eggs into Brewer's desiccation jars and replacing the normal atmosphere with carbon dioxide and a mixture of hydrogen and carbon dioxide. The embryos died within a few hours after being placed in such an atmosphere.

After incubation for various periods of time, the eggs were opened and material from them examined with the darkfleld microscope. One cubic centimeter of material was taken from those eggs showing viable organisms and inoculated into other eggs. Another cubic centimeter of egg material was taken from all eggs opened, placed into bacto fluid thioglycollate medium, and incubated for 14 days. This was examined for the presence of treponemes before being discarded.

In one experiment, 80 eggs were killed by asphyxiation in a closed container at various periods after inoculation and incubated aerobically in the egg incubator for 2 weeks. They were then opened and material from the eggs examined under darkfield microscope and inoculated into bacto fluid thioglycollate medium. None of this group revealed organisms on direct darkfield examination.

Of 61 eggs inoculated and placed in a hydrogen-carbon dioxide atmosphere and incubated for 14 to 21 days, 24 eggs (39 percent) were darkfield positive on direct examination. An additional 17 eggs (67 percent) contained viable organisms as darkfield examination of their subcultures

revealed active spirochetes. Under these conditions, the Nichols strain was cultured from egg to egg for 5 consecutive passages and maintained in eggs for 77 days.

Of 78 eggs inoculated and placed in a carbon dioxide atmosphere and incubated for 2 weeks, 19 eggs (24 percent) were darkfield positive on direct examination. An additional 31 (64 percent) proved positive upon subculture. Under these conditions, the Nichols strain was cultured from egg to egg for 5 consecutive egg passages and maintained for 81 days.

The relationship of early clinical failure to serologic response in penicillintreated early syphilis. Mark T. Hoekenga, Minerva S. Buerk and Rowland V. Rider. Am. J. Syph., Gonor. & Ven. Dis., 33: 323-333, July 1949.

The authors have examined the relationship of clinical failure to serologic response within the first posttreatment year in 15,550 persons with early syphilis. Records for the study were made available by the Syphilis Study Section of the National Institutes of Health.

In making comparisons of serologic results with immediate clinical results, the records were divided into 5 groups. Group 1 comprised 1,741 patients with seronegative primary syphilis who remained seronegative during the first posttreatment year. The cumulative clinical failure rate was 5.5 percent at the end of 18 months and 9.7 percent at 36 months. In group 2 with 7,348 patients with seropositive early syphilis (primary and secondary) who attained confirmed seronegativity within the first year, the cumulative failure rate was 3.1 percent at 18 months and 7.7 percent at 36 months. In group 3 with 4,195 patients with seropositive early syphilis, still seropositive in low titer during the first posttreatment year, the clinical failure rate was 6.4 at 18 months and 12.9 percent at 36 months. Group 4 comprised 489 patients with seropositive early syphilis, still seropositive in high titer during the first posttreatment year, with 29.9 percent developing clinical failure by the eighteenth month. In group 5 there were 1,777 patients with carly syphilis who had developed serorelapse within the first posttreatment year without previous occurrence of clinical relapse. By the eighteenth month, 75.1 percent subsequently developed clinical failure. In patients still seropositive at the end of the first year and who had not shown any indication of serologic or clinical relapse, spontaneous seronegativity was attained during the second year in about 40 percent and by the end of the fourth year in about 70 percent.

The data presented show a high degree of correlation between serologic response in the first posttreatment year and the probability of clinical failure in persons with early syphilis treated with penicillin. When serologic response was favorable, the cumulative failure rates were low.

The authors suggest that for seronegative primary or seropositive early syphilis, re-treatment need not be given if the patient remains, or becomes and remains, seronegative. In seropositive early syphilis, re-treatment need not be given because of the persistence of a weakly positive test during the first 12 months after treatment, but if the serologic test persists in high titer for 6 months, re-treatment should be given regardless of whether clinical relapse has or has not yet appeared. Patients with scrologic relapse should in all cases be re-treated as soon as the fact of such relapse is confirmed by a check serologic test.

Penicillin treatment of late neuro-syphilis—one- to five-year follow-up with special reference to clinical failures. David Landau, Israel Kopp, Augustus S. Rose and Harry C. Solomon. Am. J. Syph., Gonor. & Ven. Dis., 33: 357–363, July 1949.

In the 5-year period between February 1944 and February 1949, 446 patients with neurosyphilis were treated at the Boston Psychopathic Hospital. Of these, 52 died, 17 were lost from observation, while 377 remain in the follow-up series. Of the 52 deaths, 33 died within the first year

of treatment. General paresis was considered a contributing factor in the death of 16 patients.

One-fourth of the patients were treated with penicillin alone, while the remainder received penicillin in combination with fever therapy. From February 1944 to June 1945, penicillin was given intramuscularly in dosages of 3 million units over a period of 5 to 15 days. Thereafter, 6 million units were given in 15 days.

The criteria for evaluation of treatment were whether or not the patient was able to be out of the hospital and to be employed. If a patient had shown no material change in his condition, but was well enough to be out of the hospital and was gainfully employed or doing normal housework, he was placed in the improved group. If a patient was living at home, had shown no improvement, and was not gainfully employed, he was classed as un-A hospitalized patient was reimproved. corded in the unimproved group until he actually was in the community, even though his clinical condition may have shown improvement.

This present report is confined to 320 patients with neurosyphilis of several clinical varieties followed from 1 to 5 years. Of these, 229 (72 percent) improved, while 91 (28 percent) did not improve. Analysis of the clinical status of 233 paretic patients followed for over 1 year indicated that the type of psychosis present prior to treatment was of value prognostically. The paretic were divided into groups as to type of psychosis. Of these there was a 100-percent improvement in the manic-depressive group, 89-percent improvement in the group with minimal symptoms, 67 percent in the simple dementia group, while only 25 percent of the schizophrenic-like group When treatment was given improved. within 1 year from onset of symptomatology, 49 percent of the demented group showed some improvement.

A number of patients were treated a second or third time with penicillin. Of the 55 patients re-treated for clinical considerations, 49 percent are improved after 1 year of follow-up. Of the 20 pa-

tients re-treated on the basis of persistence of cerebrospinal fluid abnormalities or relapse, 75 percent are improved. Of the 20 living patients who were given electric shock therapy in addition to penicillin and malaria, all of the affective group are improved and at home which is in contrast to all of the schizophrenic-like group who are unimproved and are hospitalized.

The results as a whole suggest that the treatment used brought an arrest of the pathologic process to the patient followed a year or more. The lack of associated clinical improvement in some of these patients is due to neurologic residuals of the disease and to the type of psychosis present at the time of treatment.

Difficulties in the evaluation of treatment procedures in tabes dorsalis. Herbert Koteen. Am. J. Syph., Gonor. & Ven. Dis., 33: 364–379, July 1949.

The variability of the tabetic syndrome and the difficulties encountered in the evaluation of therapy are described.

From 1932 to 1948, 403 patients with tabes dorsalis were treated at the New York Hospital in the Cornell University Syphilis Clinic. Each case was reviewed, and an evaluation of efficacy of treatment was attempted, based on changes in cerebrospinal fluid and symptomatic relief. Only patients in whom subsequent lumbar punctures and physical examinations were done were used for this study. All patients were followed at least 1 year after completion of therapy. The spinal fluid was classified as improved only if the cells, total protein, and colloidal gold curve reached normal levels and if an appreciable drop in the Wassermann titer occurred. Twenty-four percent were observed for 4 years or less, 63 percent from 5 to 8 years, 8 percent from 9 to 12 years, and 3 percent for more than 12 years.

There were 49 patients in the preplanned penicillin-treated group. Of these, 33 had been treated previously with arsenicals and/or bismuth, and some with malaria, but no therapy had been received for 1 year prior to receiving penicillin. A total of 4 million units of partially purified penicillin was administered. After this regimen, the patients were seen at monthly intervals, questioned, and examined. The cell count responded promptly, the colloidal gold curve and protein responded less dramatically, while the Wassermann reaction proved most resistant to therapy. In no instance was there a relapse of cerebrospinal fluid components once normal levels had been reached. Symptomatic response varied.

Of the 125 patients who received a minimum of 50 injections of trivalent arsenicals and 25 injections of insoluble bismuth, 18 had negative spinal fluids prior to therapy. In the remaining 107 patients, 66 (62 percent) improved. No patient was treated exclusively with tryparsamide, but for the purpose of comparing the efficacy of this drug with other therapeutic agents, only those who received at least 25 injections were considered. There were 81 patients in this group, 47 of whom showed definite improvement in the cerebrospinal fluid. Of these 47, 41 had received the arsenobismuth scheduled in addition to tryparsamide. Because of absence of proof of its therapeutic efficacy and because of the dangers of optic atrophy, tryparsamide should be abandoned in syphilotherapy.

Malaria therapy was given to 48 patients, 50 percent of whom had proved resistant previously to simpler treatment schemes. The cerebrospinal fluid response was satisfactory in approximately two-thirds of the patients.

Results of this study show that there is no consistent correlation between laboratory and clinical response. of the complexities of evaluating therapy, it is difficult to recommend a single procedure that will be applicable to all pa-Tentatively, it is suggested that an initial course of 4 million units of penicillin administered over a 2-week period will give maximum benefits. there is either clinical or laboratory failure, consideration should be given to the utilization of both malaria and penicillin. The nature of presenting signs and symptoms, the duration of these symptoms, and failure to respond to previous therapeutic measures may assist the physician in anticipating which tabetic patients may derive benefits from therapy.

Aureomycin in the treatment of granuloma inguinale. Raymond C. V. Robinson, Dumont F. Elmendorf, Jr., and Harold E. C. Zheutlin. Am. J. Syph., Gonor. & Ven. Dis., 33: 389-396, July 1949.

From July 1, 1948 to March 15, 1949, 42 patients with proved granuloma inguinale were treated at the Baltimore Rapid Treatment Center. Only those patients whose lesions were found to contain Donovania granulomatis in stained scrapings or smears were accepted for study. In all instances, the lesions began on the external genitalia or in the perianal region.

Seven treatment schedules were employed. Of two administered intramuscularly, one consisted of a single daily injection of 20 mg. for a period ranging from 23 to 31 days, while the other consisted of 40 mg. three times a day for 5 days. Five schedules were administered orally. One consisted of 100 mg. three times a day for periods varying from 13 to 30 days, while another consisted of 200 mg. three times a day for 10 days. Two oral schedules consisted of 1.0 gm. four times a day, one for 5 days and the other for 10 days. One schedule was 0.5 gm. four times a day for 10 days.

Studies of the effect of aureomycin on the *D. granulomatis* were carried out in the first 19 patients, who were treated with the schedules consisting of 20 mg. of the drug, intramuscularly once a day, and 100 mg. and 200 mg. orally 3 times a day. The organism did not disappear from the lesions during the process of healing and could still be demonstrated while any ulceration was present. Since it was thought that an intensive course might give better and more lasting results, the remainder of the patients were treated with schedules of higher dosages.

As far as could be determined, there were no electrocardiographic changes, disturbance of kidney or liver function, hematologic disturbance, alterations of blood nonprotein nitrogen or sugar, or allergic reactions. There were, however,

severe local reactions to intramuscular aureomycin in all patients at the time of each injection.

Results of the study show that aureomycin, when administered intramuscularly in dosages of 20 mg. daily for 23 to 31 days, or 40 mg. 3 times daily for 5 days is less effective than streptomycin. When administered orally in total dosages of 4.2 gm. to 40.0 gm., better results were obtained with initially satisfactory clinical responses in 27 of 36 patients. In spite of the effect of the drug in healing the lesions of granuloma inguinale, there is no demonstrable effect on the causative organism. Experience indicates the necessity for an extended posttreatment observation period of at least 60 days before judging the therapeutic efficacy.

ANN. DE DERMAT. ET SYPH., PARIS

Hyperintensive treatment of recent syphilis (daily peniciliin, bismuth and mercury).

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*Treatment of early syph:lis with peniciliin. Report on three hundred and twenty-four patients treated with 1,200,000 units over seven and one-half days. Robert L. Barton, Theodore J. Bauer, Robert M. Craig and George X. Schwemlein. 60: 150-154, Aug. 1949.

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Treatment of early syphilis with penicillin G. Administration of penicillin G in peanut oil and wax twice weekly for eight weeks. Loren W. Shaffer and Charles J. Courville. 60: 253-260, Aug. 1949.

Treatment of early syphilis with penicillin. Report on three hundred and twenty-four patients treated with 1,200,000 units over seven and one-half days. Robert L. Barton, Theodore J. Bauer, Robert M. Craig and George X. Schwemlein. Arch. Dermat. & Syph., 60: 150-154, Aug. 1949.

In December 1944, a study was launched for the purpose of determining the efficacy of a schedule of treatment in which an aqueous solution of sodium penicillin was administered intramuscularly every 3 hours, 20,000 units per injection for a total of 60 injections or 1,200,000 units of penicillin. The period of treatment extended over 7½ days.

This schedule of treatment was used on 324 patients with darkfield-positive syphilis from December 1 through July 23, 1945.

The age of these patients ranged from 8 to 48 years, 19.4 percent being under 20 years, 35.5 percent from 20 to 24 years, and 45.1 percent being 25 years and over.

Of the entire group, 257 patients had received no previous treatment for syphilis. The 67 remaining patients had received some type of antisyphilitic treatment prior to their present admission and had subsequently evidenced relapse or inadequate resolution of their initial lesions.

The cumulative failure rate was 10.6 percent among 36 patients with primary seronegative syphilis, 21.9 percent among 69 patients with primary seropositive syphilis, 35.7 percent among 176 patients with untreated secondary syphilis, and 37.5 percent among 43 patients who had had previous treatment and subsequently showed infectious relapse. The cumulative over-all failure rate, regardless of

diagnosis, was 29.6 percent at the end of 1 year's observation.

One hundred and seventy-one (59.4 percent) of the seropositive patients achieved seronegativity during the year after treatment. Sixteen (9.4 percent) of these subsequently relapsed.

For 60 of the total number of patients treated, the result was known to be a failure. Since it is futile to attempt to separate reinfection from relapse all recurrences of syphilis are grouped as treatment failures.

ARCH. F. D. GES. VIRUSFORSCHUNG, VIENNA

Beitrag zur pathologischen anatomie und zur pathogenese der recitis poradaenica (lymphogranulomatosis inguinalis oder Nicolas-Favresche krankheit). (Observations on the pathology of lymphogranuloma inguinale (Nicolas-Favre disease)). R. Jaffe. 4:63-74, June 30, 1948. [Abstracted in Bull. Hyg., London, 24:324, May 1949.]

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Mod. Concepts Cardiovas. Dis., New York Heart disease and pregnancy. Part II. [Syphilis.] Julius Jensen. 18: 33-34, Feb. 1949.

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Scrvice by State and Territorial Health Departments, April to June 1949

[Known military cases excluded]

		prior	Private physi- cian sources	1.05 1.04 1.04 1.29 (*) 1.28	1.05 (*) 1.10 1.04 1.11	.92 .89 .89 .92 1.06	1.00 1.24 1.06 .89	.93 .79 .80 .1.53
	Gonorrhea	Ratio to prior quarter	All sources s	1.04 1.05 1.35 1.04 (*) (*)		1.06 1.08 1.14 1.09 1.09	1.03	. 99 . 98 . 99 1. 04 1. 28
	Ö	Total all sources		1, 023 215 93 590 13 71	9, 723 47 1, 016 6, 017 5, 113 2, 643 2, 369 2, 369	13, 345 3, 698 1, 854 1, 572 3, 819 2, 722 1, 252	6, 356 1, 452 2, 245 2, 659	7, 221 6, 132 4, 855 702 240 147
	d	Ratio to prior quarter	Private pbys:- cian sources	*:*:*: *:*:*:	(*) (*) 1:24 1:24 0 0	€€€€1€1	1.04	11111
	Not stated	Ratio t qua	All	0.96 (*) (*) (*) (*) (*) (*)	. 67 . 44 1.03 . 97 . 87 . (*)	60 63 54 59	1.05 (*) 1.03	() ()
		E	rotai all sources	113 34 34 0 0 0 0 0 40 39	143 18 39 86 66 0 0	45 24 20 20 10 0	225 14 211 0	0000
		o prior	Private physi- cian sources		(*) (*) (*) (*) (*) (*) (*)	# 100000	1.03 (*) (91 1.02	1.30
	Congenital	Ratio to prior quarter	All		(*) (*) 1. 45 1. 51 1. 11 (*)		1.04 1.22 1.02 1.00	1.05 .90 .87 1.06 (*)
3		Total all sources		75 111 10 34 22 122 6	44 44	314 16 61 31 106 45 86	342 50 198	251 106 54 94 13
`	atent	Ratio to prior quarter	Private physi- cian sources	1.10 (*) 1.32 (*) (*) 1.04 (*)	(*) (*) (*) 1.13 1.10 1.77	1.25 1.15 1.15 1.30 1.31 1.31 1.53	. 96 . 79 1. 07 . 96	1. 12 1. 00 1. 03 . 95 . 95 2. 16
Syphilis	Late and late latent		All	1.06 .81 .93 1.14 (*) 1.13 (*)	1.03 47 95 1.04 1.10 1.59	1.09 1.05 1.01 1.01 1.01 1.47	. 98 	1.07 1.00 1.02 1.02 1.00 2.01
	Late a	Total all sources		653 86 38 366 122 122 16	6, 780 36 1, 138 4, 290 3, 294 1, 316 941	2,661 358 930 699 313 424 636	3,896 454 1,166 2,276	3, 047 1, 788 1, 950 574 473
	ıt	o prior ter	Private physi- cian sources	1.05	1.13 1.08 1.10 1.18 1.26 1.04	1.23 (*) 1.62 (*) 1.38 1.24 1.07	. 95 87 98 98	. 95 . 83 . 82 1.00 (*) (*)
	Early latent	Ratio to prior quarter	All	1.13 1.30 (*) 1.21 (*) 1.09 (*)	. 95 . 95 . 99 1. 03 1. 03 1. 02 . 95	. 99 . 98 1.11 1.02 1.03 1.10	. 83	. 90 . 85 . 92 1. 58 1. 22
	E	Total	all sources	226 57 57 99 99 6	3, 116 82 629 1, 266 1, 198 1, 139 839 99	2, 451 231 545 326 714 612 349	2, 105 280 443 1, 382	1, 536 982 708 380 52 122
	ondary	1	Private physi- cian sources	0.76 (*) .92 (*) .83	(*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	. 91 (*) . 56 . 36 1.17 1.17	1.12 1.12 1.81 1.70	. 80 . 78 . 80 . 81 (*)
	Primary and secondary	Ratio to prior quarter	All	0.80 .57 .78 (*)	. 73 . 39 . 66 . 88 . 86 . 65 . 47	883 779 883 883 893 893	.87 .87 .80 .71	.84 .88 .88 .88 .88 .88
	Primary	Total all sources		225 255 102 10 16	1, 248 22 178 696 581 352 161 43	1, 544 166 349 221 504 287	926 229 300 397	919 649 408 191 20 59
		Federal Security Agency regions		Region 1—Total Connecticut Maine Massachusetts New Hampshire Rhode Island Vermont	Region 2—Total Delaware New Jersey New York New York Pennsylvania Philadelphia	Region 3—Total District of Columbia. Maryland Baltimore North Carolina. Virginia.	Region 4—Total Kentucky Michigan Ohio	Region 5—Total b

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2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2	10, 751	10, 914	when base is less than 30. Base is zero or unknown
Region 6—Total Alahama Alahama Georgia Mississippl. South Carolina Tennessee Puerto Rico Virgin Islands Region 7—Total Kansas Ransas North Dakota South Dakota South Dakota South Dakota South Dakota Calisana North Dakota South Dakota South Dakota South Dakota South Dakota Calisana North Dakota South Dakota California Arkansas Louisiana California Manana Utah Wyoning Region 10—Total Arizona California Nevada California Nevada California Nevada Canal Zone	Continental United	Total United States including Territories buries	* Ratio not calculated when base is less than 30, — Ratio not calculable. Base is zero or unknow

Source: Form 8958-B FSA-PHS—Division of Venereal Disease, 11/4/49 (ML-MC)mw. * Ratio not calculated when base is less than 30.

— Ratio not calculable. Base is zero or unknown.



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FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE



Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948.

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription Price: Domestic 75 cents a year; foreign \$1.15



Editorial

Dr. John F. Mahoney retires from the Public Health Service.

Last month, Dr. John F. Mahoney retired from the United States Public Health Service and from his position as director of the Venereal Disease Research Laboratory. To all of us in the Division of Venereal Disease his retirement presents a sharp reminder of the gratifying gains made in venereal disease control in recent years; and we are so reminded because he has long been closely allied with these gains through his brilliant and progressive contributions in the fields of basic biology, serology, therapy, epidemiology, and applied research. We shall long remember his work, his vitality, and the stimulation of our association with Dr. Mahoney. We at once envy and congratulate the City of New York and its people, whom he will serve, and serve well, as Commissioner of Health.

In July 1929 Dr. Mahoney became director of the newly created Venereal Disease Research Laboratory, and under his guidance the investigative work encompassed and solved a multiplicity of fundamental scientific problems. The scope of his work and ideas has been too broad to recount fully here, but the influence of his contributions has been recognized nationally and internationally.

Dr. Mahoney's name, in the minds of most persons, has been and will perhaps most often be connected with his preliminary study on penicillin in syphilis, and rightly so. He made a tentative prediction then that "a rebuilding of the structure of syphilis therapy may become necessary." The rebuilding did indeed become necessary, bringing with it an era of medical progress that has surpassed the one introduced by Ehrlich with the arsphenamines. In 1946, his contributions to the conquest of syphilis won for him the Lasker Award of the American Public Health Association.

His associates and fellow scientists salute John Mahoney's contributions and leadership in syphilis serology, in experimental syphilis, in immunology and biology, in medical epidemiology and prophylaxis of syphilis and gonorrhea, and in the further development and application of the antibiotics.

Dr. Mahoney is chairman of the Expert Committee on Venereal Diseases of the World Health Organization. He is also chairman of the National Advisory Serology Council. He is a member of the National Research Council and has been awarded a life membership in both the Association of Military Surgeons and the American Social Hygiene Association.

We in the Division of Venereal Disease and in Public Health Service have valued his friendship, his remarkable skills, and his warm person ality. We are glad that he has chosen to remain in the field of public health. To Dr. John F. Mahoney we express our gratitude for more than 30 years of extraordinary service—the kind of service that permits us to look forward to true control of the venereal diseases in this country and throughout the world.

Theodore J. Bauer, Medical Director Chief, Division of Venereal Disease

Filter Paper Miscroscopic Test for Syphilis, or the FPM Test

A Preliminary Report

Ralph B. Hogan, Senior Surgeon,¹ and Shirley Busch, Bacteriologist,² United States Public Health Service

The standard serologic tests that have been developed and used in this country require clear serum for their performance. The amount of serum required varies from 0.05 cc. to 0.5 cc., which necessitates venipuncture for collection of blood. The only exception described among the standard tests is the Davies-Hinton microflocculation test, in which the blood may be collected in a capillary tube and may be obtained from a finger prick or from the toe, heel, or ear lobe. Although this method appears simple, 0.15 to 0.2 cc. of blood is required, and the collection of this amount, particularly from infants, is sufficiently difficult that the method has never become highly popular.

A simpler method of collecting and testing blood would be useful for diagnostic activities in general, and would be particularly desirable for the diagnosis and treatment control of congenital syphilis in infants. Indeed, the nonavailability of such a simple procedure has hampered the congenital syphilis control program.

Although there has been a steady decline in the morbidity reporting of primary and secondary syphilis, the number of cases reported as congenital syphilis has remained constant for the past 5½ years. Furthermore, only one-fifth of the congenital syphilis reported is found in children under 1 year of age, with four-fifths going into later years; most cases are not discovered until elementary school or high school. One of the greatest obstacles to finding and treating early congenital syphilis is the technical difficulty

of obtaining a satisfactory sample of blood from infants.

In the field and in the small clinic, lack of adequate facilities often makes it difficult if not entirely impracticable to perform jugular punctures. Because of the difficulty of collecting blood for the standard tests under the field conditions prescnt in Cuba, Chediak (1) developed a technic in the early 1930's for performing a serologic test with dried blood. Later, a modification of the Chediak test was described by Zimmermann, in which the blood was collected by absorption on a small piece of filter paper (2). Although these tests have not been as satisfactory as the standard serologic tests, they have apparently fulfilled a need.

This paper, using the concept of the Zimmermann and the Chediak tests, describes a recently developed test that uses whole blood obtainable from a finger prick. Inasmuch as this new test is read miscroscopically and is designed to utilize whole blood which is collected and dried on filter paper, it seems reasonable to refer to it as the filter paper microscopic test (FPM test).

Methods

Antigen

The VDRL antigen ³ was selected as the basic antigen in order to take advantage of the desirable features of a cardiolipin antigen (3, 4). Preliminary experiments indicated that the sensitivity of this standard cardiolipin antigen was comparable to lipoidal antigens when subjected to whole blood.

¹ Chief, Clinical and Laboratory Research Branch, Division of Venereal Disease.

² In charge of the Serology Laboratory, Eastern Medical Center, Durham, N. C.

³ As used and standardized at the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y.

Filter Paper

A good quality paper, relatively thin and smooth so as to permit one or several pieces of paper to lie flat and to occupy the smallest possible volume, was considered essential. The Eaton and Dikeman filter paper No. 613 fulfilled these requirements. The paper was cut into strips 7 inches in length and $\frac{3}{8}$ of an inch wide. One and one-half inches of this paper absorbed 0.05 cc. of whole blood. Variations of less than $\frac{1}{4}$ inch occurred from specimen to specimen.

Blood that was weakly positive to the ·standard serologic tests was absorbed on strips of filter paper and allowed to dry. Pieces of this dried paper three-eighths of an inch square, when extracted with normal saline solution and the saline extract then tested with the regular VDRL antigen, were found to give negative reactions. In order to increase the sensitivity, four adjustments could readily be made: (1) increase the amount of dried blood, (2) increase the electrolyte concentration (concentration of saline solution), (3) reduce the amount of antigen in relation to the amount of blood, and (4) increase the sensitivity of the antigen by increasing the lecithin content.

Titrations for Optimum Conditions

1. Titration for optimum antigen sensitivity.—By increasing the lecithin content by increments of 0.02 percent, it was found that maximum sensitization was obtained at approximately 0.34-percent lecithin (table 1).

Table 1.—Titration for optimum antigen sensitivity — results obtained when dried blood (weakly positive by the standard Kahn test) was extracted with 1.5-percent saline solution and the extract tested with antigens of varying lecithin content

Percent leci-	0.20	0.22	0.28	0.32	0.34	0.36
Result	N	WP	P	P	SP	P

N=negative P=positive WP=weakly positive SP=strongly positive 2. Titration for optimum salt concetration (using three pieces of paper). Concentrations of salt from 0.9 to 1.8 percent regularly gave clean negative is sults with known-negative bloods, usi antigens of varying lecithin content (take 2). Occasionally a specimen of negation blood was found to give a somewhard rough-negative reaction at 1.8 percent 2-percent concentration and in except of 2 percent, the negatives appeared rough most instances.

Table 2.—Titration for optimum s concentration (3 pieces of paper) results obtained when dried blo (negative by standard tests) was e tracted by various concentrations saline solution and tested with an gens of varying lecithin content

Percent lecithin	Perce	ent salin	ie soluti	on used	for extr	actic
in antigen	0.9	1.2	1.5	1.8	2.0	4.
0.20 .22 .28 .32 .34	N N N N N N N N N N N N N N N N N N N	ZZZZZ	ZZZZZ	ZZZZZ	RN RN RN RN	RI RI RI RI

N=negative RN=rough-negative

3. Titration for optimum extraction. Using a weakly positive blood, the opmum time of extraction was determin with 0.2 cc., 0.15 cc., and 0.1 cc. of 1.5-pecent saline solution (table 3). More th 20 minutes was required for optimu extraction. Greater sensitivity was extractined with the smaller quantities extracting solution.

The optimum sensitivity of the antig was found to occur at a concentration 0.34-percent lecithin. Increasing the seconcentration from 0.9 to 1.8 percent denitely increased the sensitivity without interfering with clear-cut negatives. The 1.5-percent saline solution appeared provide a reasonable margin of safety a was therefore selected for preliminatival. Satisfactory sensitivity was etained with three pieces of paper of tracted with 0.1 cc. of saline solution Using the highly sensitized antigen (0.5 percent lecithin), three pieces of paper and 0.1 cc. of 1.5-percent saline solution

Table 3.—Titration for optimum extraction—results obtained when 1, 2, and 3 pieces of paper (weakly positive blood) were each extracted with 0.1, 0.15, and 0.2 cc. of 1.5-percent saline solution for 10, 20, and 40 minutes

Amount of saline solution	Number of pieces of paper extracted for 10 minutes			Number of pieces of paper extracted for 20 minutes			Number of pieces of paper extracted for 40 minutes		
	1	2	3	1	2	3	1	2	3
0.2 cc .15 cc .1 ec	RN RN RN	RN RN WP	RN WP WP	RN RN RN-WP(?)	W.b W.b	WP WP WP	RN RN WP	RN WP WP	WP WP P

P=positive. RN=rough-negative. WP=weakly positive.

test bloods giving weakly positive reactions of one Kahn unit (KU) with the standard Kahn test were found to give from weakly positive to fully positive reactions when tested with this technic. The test negatives were clean and clearcut.

Results of Clinical Trial

1. Preliminary Results

(a) Using cardiolipin antigen sensitized with 0.32- or 0.34-percent lecithin, three pieces of filter paper three-eighths of an inch square, and 0.1 cc. of 1.5-percent saline solution with 30 minutes extraction:

A total of 610 tests were completed. Seventy disagreed in some way with either the findings of the standard Kahn test or of the standard VDRL test. Twenty-one of these were weakly positive with the filter paper test and negative with the standard tests. Forty-nine were insensitive. Twenty-three, however, showed less than 4 KU with the standard Kahn test; six had titers of 32 or more KU. Heating the papers in dry heat (56° C. for 30 minutes) failed to produce positive results on those bloods that had shown high titers by the Kahn test and negative reactions by the FPM test. Heating the papers did not appear to increase the number of positives or the degree of flocculation. The sensitivity was obviously unsatisfactory, particularly from the standpoint of the high titers.

(b) Using the regular VDRL antigen (0.2-percent lecithin), three pieces of paper three-eighths of an inch square, and

0.1 cc. of 1.5-percent sodium chloride with 30 minutes extraction:

A better antigen-antibody ratio was found to exist when the regular VDRL antigen was used in place of the highly sensitized antigen. Among the next 365 cases tested, there were 36 discrepancies between the FPM test and the standard Kahn test or the standard VDRL test. Of these 36 discrepant reactions, 25 (negative by the standard tests) were weakly positive by the FPM test, and 11 (positive by the standard tests) were negative by the FPM test. However, 8 of the 11 had low titers of 3 KU or less. On the other hand, one positive blood (2,084 KU) was negative repeatedly by the FPM test. Of the 25 weakly positive reactions, information was available in 10 cases—4 represented syphilitic patients treated from 1 to 4 years previously; 1 was a case of primary syphilis; 1, secondary syphilis; 1, chancroid: and 3 had been diagnosed as having no venereal disease. Although a majority of the weakly positive reactions may have represented true reagin, nevertheless, in view of the number of weakly positive reactions and the occasional zone-type reaction obtained, a further change was made in the test procedure. A reduction in the saline concentration from 1.5 to 0.9 percent was introduced in order to reduce the number of weakly positive reactions. To compensate for the expected reduction in sensitivity, a larger amount of blood (4 pieces of paper) was used in the test. A second test was performed simultaneously, using only 1 piece

of paper in order to detect as many zone reactions as possible.

2. Final Results

Using the regular VDRL antigen, four pieces of paper (0.05 cc. of blood) and one piece of paper (0.0125 cc. of blood) simultaneously, and 0.1 cc. of 0.9-percent sodium chloride extracted for 30 minutes:

Seven hundred and thirty-five tests ⁴ have been performed with this final technic. Included in this series were 463 positives and 272 negatives by the standard Kahn test.⁵ Approximately 150 of these tests were performed on bloods which had previously shown some discrepancy between results obtained with the FPM test and with either the standard Kahn test or with the VDRL test when the for-

mer had been performed with the hig sensitized antigen and 1.5-percent sal solution. There were 16 discrepand (2.2 percent) between the FPM test a either the standard Kahn test or VDRL test (table 4).

Eight weakly positive reactions tained with the FPM test were negated by either the Kahn or VDRL tests, a eight negative reactions were positive either the Kahn or the VDRL tests. For these latter reactions had low titers two Kahn units or less.

Aside from case 520, on which no interaction is available, the clinical findicand histories tend to suggest that Kahn test may have been in error seven cases, while the FPM test appet to have been in error in eight cases.

Table 4.—Total discrepancies between the FPM and either the Kahn or the VD tests (final technic)

Cana Na	Result h	y serologi	c teehnie	Clinieal findings and history				
Case No.	VDRL	Kahn	FPM					
62-238-244-271-381-420-427-430-439-4489-489-	WP ND N N ND	4 N N N 8 N 1+ 8 2 N N	N WP WP WP N WP N N WP	2-month-old infant. Mother had positive STS. Treated for primary syphilis in Octoher 1942—no darkf Primary syphilis, darkfield positive. Injections given in 1948—questionable syphilis. Treated for latent syphilis in 1948. No history of syphilis. No history of syphilis. Treated for early latent syphilis in 1949; also in 1946. Treated for early latent syphilis in 1949. Treated for eongenital syphilis at 15 years of age in 19 Genital lesion, darkfield negative.				
495 520 610 622 636	N N ND ND ND	N N 1+ 2+ D-	WP WP N N	Treated for syphilis in April 1949. Treated for early latent syphilis in 1939. Primary syphilis, darkfield positive. Treated for primary syphilis, darkfield positive, in 19				

ND=no data.

N = negative.

WP=weakly positive.

D=doubtful.

Technic of the FPM Test

General Equipment (fig. 1)

- 1. Rotating machine—Boerner-type.
- 2. Humidifier.
- 3. Knife or scissors.
- 4. Hypodermic needles, 23-gage, 10 bevel.
- Strips of filter paper % of an in wide, 7 inches long, Eaton and Di man No. 613.

⁴ The bloods were obtained from school examinations performed by the Durham City and County Health Department and from patients admitted to the Durham City and County Health Department and to the Eastern and Western Medical Centers.

⁵ The comparison of the performance of the FPM test with the standard Kahn test was possible through the cooperation of the Durham City and County Health Department, the Western Medical Center, Charlotte, N. C., and the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island 4, N. Y.

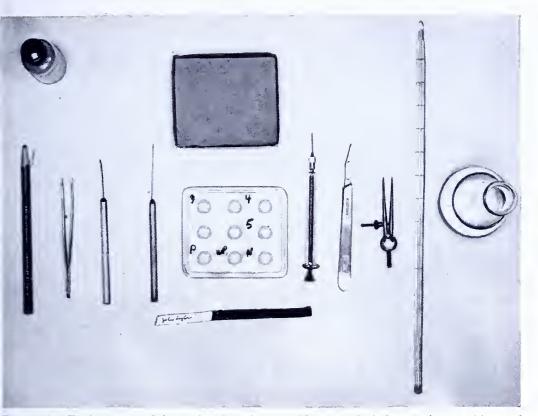


FIGURE 1.—Equipment used in performing the test (does not include rotating machine and microscope).

- 6. Two straight, dissecting-type needles.
- 7. Thumb forceps—blunt, square-tipped.

Glassware (fig. 1)

- 30-ml. bottles, glass-stoppered or screw-capped, with vinylite or tinfoil lining.
- 2. Syringe, Luer-type, 1 to 2 ml.
- 3. Glass plate, pyrex, 3½ by 4 inches.
- with nine concavities 3/4 inch in diameter by 1/2 inch in depth.

Preparation of Antigen

The antigen is the regular VDRL antigen utilized in the VDRL slide flocculation test (5).

Preparation of Saline Solution

- 1. Buffered saline solution containing 1-percent sodium chloride for diluting antigen is prepared as for the VDRL test (5).
 - 2. The 0.9-percent saline solution used

for extraction is prepared by adding 900 mg. of dry sodium chloride (reagent grade) to each 100 ml. of distilled water.

Preparation of Antigen Emulsion 7

- 1. Pipette 0.4 ml. of buffered saline solution to the bottom of a 30-ml. round, glassor screw-cap stoppered bottle.
- 2. Add 0.5 ml. of antigen (from the lower half of a 1.0-ml. pipette graduated to the tip) directly onto the saline solution while continuously but gently rotating the bottle on a flat surface.

Note: Antigen is added drop by drop, but rapidly, so that approximately 6 seconds are allowed for each 0.5 ml. of antigen. Pipette tip should remain in upper third of bottle, and rotation should not be vigorous enough to splash saline solution onto pipette.

3. Blow last drop of antigen from pipette without touching pipette to saline solution.

⁶ Corning Glass Co.—pyrex plate 7220.

 $^{^{7}}$ Manual of Serologic Tests for Syphilis (5), p. 110.

- 4. Continue rotation of bottle 10 more seconds.
- 5. Add 4.1 ml. of buffered saline solution from 5.0-ml. pipette.
- 6. Place top on bottle and shake vigorously for approximately 10 seconds.
- 7. Antigen emulsion is then ready for use and may be used during 1 day. This amount (5.0 ml.) is sufficient for approximately 250 serum tests.

Twice this amount of antigen emulsion may be prepared at one time in a 30-ml, bottle by using doubled quantities of antigen and saline. A 10-ml, pipette should then be used for delivering the 8.2-ml, volume of saline solution. If larger quantities of antigen emulsion are required, more than one mixture should be prepared. These aliquots may then be pooled and tested.

Preparation of Blood

The blood may be obtained from a finger, heel, or toe puncture (fig. 2). The puncture should be made with a cutting edge to assure adequate flow of blood. Either the automatic laucet or the No. 11

Bard-Parker blade inserted into a congives satisfactory results. At least inches of the paper strip should be sat rated by touching the end of the paper to the drop of blood and then gradual moving the paper along so as to even distribute the blood over the paper strilf the quantitative test is desired, at least inches should be saturated. The striphold be laid on a clean surface to d (a paper towel is suggested).

Performance of the Test

- 1. Cut %-inch squares from the dri strip. Place four such squares in one cocavity of the pyrex plate, and place o square in a second concavity (fig. 3).
- 2. Add 0.1 cc. of 0.9-percent saline soltion to each concavity. Saturate t paper by manipulation with needles.
- 3. Cover plate with humidifier (blotti paper in humidifier should be well moi ened with water) to prevent evaporation
- 4. Rotate on rotating machine (1 r. p. m.) 15 minutes.
- Remove plate from rotator and tu paper over in liquid with aid of needle



FIGURE 2.—Method of taking the blood for the test.



FIGURE 3 .- Papers in the concavities of the pyrex plate preparatory to beginning the test.

cover with humidifier, and rotate for an additional 15 minutes.

- 6. At the end of this period of extraction (30 minutes), squeeze papers with a pair of thumb forceps to express all possible liquid. Discard papers.
- 7. Add one drop (1/60 ml.) of antigen from a 23-gage needle ⁸ to each blood specimen.
- 8. Rotate plate 4 minutes at 180 r. p. m. (covered with humidifier).
- 9. Read tests immediately after rotation. (Note: Known-positive, weakly positive, and negative serum controls are always included.)

Reading and Reporting Test Results

Tests are read miscroscopically, with low-power objective, at 100× magnifica-

tion. The antigen particles appear as short-rod forms at this magnification. Aggregations of these particles into large or small clumps are interpreted as degrees of positivity.

Reading Report

No clumping or slight Negative (N). roughness.

Small clumps (5 to 10 Weakly posiantigen particles). tive (WP). Medium and large clumps, Positive (P).

Only the terms positive, weakly positive, and negative should be used for reporting the results of this test.

Heavy rough-negatives with no definite clumping are often noticeable, particularly in highly colored extracts. Experience will allow differentiation to be made between these and weakly positive reactions in which definite clumping of antigen is present.

⁸ The needle should be held at such an angle that the bevel is downward and the dropping surface horizontal as described in the standard VDRL technic (5).

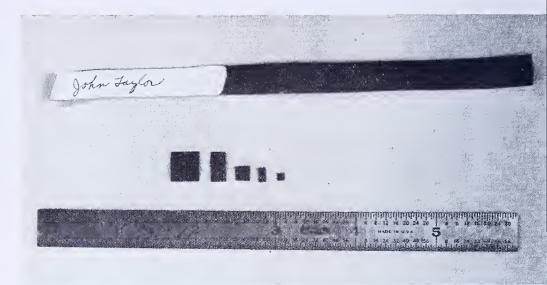


FIGURE 4.—Papers cut for quantitation.

Quantitative Test

Quantitation is obtained by performing the test on a series of decreasing amounts of paper—3 pieces, 2 pieces, 1 piece, ½ piece, ¼ piece, and so forth (fig. 4).

The titer is represented by the smallest piece of paper giving a positive or weakly positive reaction—i. e., a reaction positive with ½ piece but negative with ½ piece is reported as a titer of 8. The titer is the number obtained by dividing 4 pieces of paper (the largest number used in the qualitative test) by the number of pieces or by the fraction of 1 piece at which the reaction is either positive or weakly positive. Five illustrations of the method of calculating titer are shown in the following:

4	$\frac{N}{3}$	umber o 2	of pieces 1	of pap	er ½	1/8	m:t ou
1	1.3	Corres	pondin 4	g titer 8	16	32	Titer
P P P WP WP	P P WP WP WP	P P N WP	P WP N WP N	P N N WP N	N N N WP N	N N N N N	8 4 1.3 16 1.3

N=negative P=positive WP=weakly positive

Note: An oceasional specimen of blood will give only a weakly positive reaction throughout its quantitation,

Summary

- 1. This paper describes a flocculation test for syphilis that uses whole bloom (collected on filter paper and dried) of tainable from the puncture of a finge heel, too, or ear lobe, thus obviating the need for performing jugular punctures it infants and children.
- 2. The standard VDRL antigen is use to perform the test.
- 3. As described in the text, the test-using 4 pieces of paper (0.05 cc of blood and 1 piece (0.0125 cc. of blood) simultaneously, the standard VDRL antigen, and 0.1 cc. of 0.9-percent saline solutionshows promise of sufficient sensitivity and specificity that its use as a standart test may be possible.
- 4. The test is not presented as "quickie." It requires approximately a much time to perform as is required the standard slide tests.
- 5. The test is not designed for office us It requires technical skill comparable the standard tests.

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The Newer Antibiotics in the Therapy of the Venereal Diseases Other than Syphilis¹

Robert B. Greenblatt, M. D., Virgene S. Wammock, M. D., Calvin H. Chen, M. D., Robert B. Dienst, Ph. D., and Robert M. West, B. S.

A review of the present status of the newer antibiotics in the therapy of the venereal diseases other than syphilis is in order. There are now three effective antibiotics in the treatment of granuloma inguinale—streptomycin (1), aureomycin (2), and chloromycetin (3). Chancroid, gonorrhea, and fusospirochetosis are favorably influenced by these antibiotics, and it appears that aureomycin and chloromycetin hold some promise in the management of lymphogranuloma venereum.

Granuloma Inguinale

Streptomycin

Streptomycin was the first antibiotic to offer hope for the cure of the patient with granuloma inguinale. Barton, Craig, Schwemlein, and Bauer (4) reported a

This study was aided by grants from the State of Georgia Department of Public Health and the U. S. Public Health Service.

good result in 1 case and failure in 2 pa-Greenblatt, Kupperman, Dienst (1) tried various dosage schedules and found the minimum effective dose of streptomycin to be 20 gm, administered over a period of 5 days. When this schedule was employed in 95 of 142 patients treated, a cure rate of about 90 percent was obtained. When larger doses were employed, i. e., 4 gm. a day for 10 days or longer, the failure rate was reduced even further. However, if doses of less than 2 gm. a day were used over periods of time ranging from 6 to 62 days, the relapse rate was 25 percent. Five streptomycin-resistant cases were encountered. These patients had received from 40 to 158 gm. of the drug without benefit. The advantage of streptomycin is the shortness of the period necessary for treatment. The disadvantages are parenteral administration, the need for hospitalization, and occasional severe untoward reactions.

Aureomycin

Aureomycin was employed by the authors in the treatment of 47 patients with granuloma inguinale. When aureomycin

¹ From the University of Georgia School of Medicine, Augusta, Ga.

Read at the Eighth Semi-Annual Venereal Disease Control Seminar, U. S. Public Health Service, Regions VI and VIII, Savannah, Ga., September 28, 1949.

was first introduced, it was available in solution for parenteral use. Four patients were so treated, receiving total doses varying from 420 to 1,500 mg. in 7 to 23 days. In no instance was healing accomplished, nor was there a disappearance of Donovan bodies from the lesions. Subsequently these 4 patients responded satisfactorily to the oral administration of the drug. These results are not in accord with the findings of Wright et al., who reported 2 cures in granuloma inguinale treated intramuscularly with 2,020 and 560 mg., respectively (5). streptomycin-resistant patients previously mentioned readily healed with oral aureomycin medication (2). Varying dosage schedules were tried. It was soon established that the minimum effective dose of oral aureomycin necessary for cure was 20 to 25 gm. administered in 500-mg. doses every 6 hours over a period of 10 to 12.5 days. When larger individual doses were used, nausea was common, and this will be discussed under side effects. The 20- or 25-gm, dosage schedule was undertaken in most instances, but if the lesions appeared refractory or the lesions were responsive but remained incompletely healed after several weeks, the dosage was continued or another course of therapy given until healing was complete or seemed assured. In such instances, between 30 and 70 gm. of the drug were used. Only 1 patient was healed with less than 20 gm., and this patient received only 10.8 gm. in 20.5 days. has remained well for the past 10 months.

Relapses.—Only those patients whose lesions healed completely but subsequently broke down were considered as relapses. One occurred in a patient treated with 1 gm. every 6 hours to a total of 20 gm. This patient later admitted to having vomited part of her drug. She did not mention this at the time for fear of prolonging the period of hospitalization. She was successfully re-treated with 20 gm. in 10 days and has now remained well for an additional 6 months. The only other relapse that occurred among the 47 patients treated with aureomycin took place

in a patient who had originally received 25 gm. within a period of 12.5 days. The lesions in this case were healed upon completion of treatment; however, the patient returned in 4 weeks with a small relapsing lesion of 4 days duration. Donovan bodies were demonstrated, and the patient was successfully re-treated with an additional 25 gm. He has now remained well for 2 months.

Chloromycetin

Chloromycetin was administered to 34 patients with granuloma inguinale and has proved as effective against granuloma inguinale as aureomycin has. It has the added advantage of almost complete lack of side effects. In all but 3 cases we have arbitrarily given the drug as 500 mg every 6 hours. The first 3 patients were treated with 1 gm. every 6 hours to a total of 20 gm. in 5 days. Because 1 re lapse occurred in this group, it was decided to prolong therapy and give only a 500-mg. individual dose in subsequen patients and thereby make the schedule comparable employed to that with aureomycin,

Relapses.—Two relapses occurred in this series. One took place 2.5 months after the patient had completed therapy with 20 gm. of chloromycetin. This patient was pregnant, and the relapse occurred at the time of delivery. She was uccessfully re-treated with 20 gm. in 10 days. The other relapse took place in a patient with slow response to the original course of 50 gm. in 20 days. This relapse also occurred 2.5 months after completion of the original course of treatment, and she was successfully re-treated with an additional 20 gm. in 10 days.

Lymphogranuloma Venereum

Lymphogranuloma venereum does not respond to either penicillin or streptomy cin (5). The lesions of this disease do however, respond slowly to treatment with both aureomycin and chloromycetin. The response to aureomycin was first reported by Wright, Sanders, Logan, Prigo and Hill (6).

Aureomycin

Aureomycin in our hands has proved of more value than chloromycetin has, late we have treated 26 lymphogranuloma venereum patients with aureomycin. Phirteen of these had manifestations of early lymphogranuloma venereum, as evidenced by primary ulcers and/or buboes. Ulcers of late lymphogranuloma venereum, rectal strictures with or without proctitis, and multiple-draining sinuses of long duration, resistant to treatment with chloromycetin, are included in this group.

The results in early lymphogranuloma venereum were considered good in only 4 of the 13 patients. These results are rather equivocal, inasmuch as we observed from time to time patients in whom the buboes subsided without therapy. It is our experience that aureomycin offers little advantage over the sulfonamides in the treatment of patients having early manifestations of lymphogranuloma venereum, with the exception that the former is less toxic.

Two patients with multiple-draining sinuses of the penis, scrotum, and adjacent areas, of 2 years' duration have been treated with 75 and 100 gm. of aureomycin, respectively, as a total dose and have both shown marked improvement. Lesions in both of these patients had improved slightly and then relapsed following 40 and 100 gm. of chloromycetin.

Eleven patients with late manifestations of lymphogranuloma venereum presented rectal strictures and/or proctitis or ulcers. It was necessary to stop treatment in two patients because of severe vomiting. Fibrotic strictures of long standing do not respond to any of the antibiotics or sulfonamides. However, inflammatory strictures do respond if daily digital dilation is done during the course of aureomycin therapy. This procedure, if religiously followed, would preclude the necessity for colostomies in many of Proctitis of late lymphothese cases, granuloma vencreum responds to large doses of aureomycin over a prolonged period of time. The discharge had stopped upon completion of treatment in only three patients who received as little as 20 gm. or less. In four cases it was necessary to give 75 to 100 gm. in 37 to 60 days before marked improvement was noted. In our experience, ulcers of late lymphogranuloma venereum did not seem to respond to aureomycin therapy, while proctitis and inflammatory strictures appear to respond well to prolonged treatment.

Chloromycetin

Chloromycetin was employed in the treatment of 11 patients with lymphogranuloma venercum. Buboes and/or primary lesions of this disease were present in 4 cases. The response was not considered good in any of these cases, and in our considered opinion chloromycetin is not equal to aureomycin in the management of patients having this type of involvement. The series, however, is too small to draw definite conclusions.

The two patients previously mentioned who had multiple-draining sinuses due to long-standing infection with lymphogranuloma venercum showed slight improvement upon completion of therapy with 40 and 100 gm. of chloromycetin, respectively. However, within 2 weeks both relapsed, and the amount of purulent discharge in each was considerably worse than on first admission. The lesions in both subsequently responded well to aureomycin.

Chloromycetin therapy was employed in five patients having proctitis and rectal strictures. This group, again, is too small to draw definite conclusions; however, it appears that aureomycin is superior to chloromycctin in the treatment of patients with any type of involvement due to lymphogranuloma venereum. The only patient who had complete cure of her proctitis under chloromycetin therapy was unable to tolerate aureomycin even in doses of only 250 mg. Therefore, chloromycctin is of value in the patient who cannot take aureomycin, and its use should, perhaps, be reserved for patients in this category.

Chancroid

Penicillin is of little or no value in the treatment of chancroid, although improvement has been noted after its use (7, 8). The lesions, however, do respond to streptomycin, aureomycin, or chloromycetin. Streptomycin in vitro appears to be the most effective of these anti-Hirsh and Taggart (10) biotics (9). showed streptomycin to be effective clinically against chancroid; however, 5 to 25 gm, were necessary for cure. As small a total dose as 5 gm. of aurcomycin given within a 5-day period has effected cure of lesions of chancroid which had not responded to 1 weeks' treatment with sulfonamide drugs (11). Five to ten grams of chloromycetin are necessary for the cure of chancroid. One of our recent patients with a large chancroid lesion responded well to 10 gm.

Gonorrhea

Both aureomycin (12) and chloromycetin (13) have been used with success in the management of gonorrhea. The oral dosages employed for either antibiotic were 1 gm. 3 times a day for 1 or 2 days (i. e., 3 or 6 gm.). In the case of aurcomycin, the 3-gm. dosage seems to be as good as that of 6 gm.; whereas, in the case of chloromycetin, the 6-gm. dosage is better. Since the number of cases included in our studies is limited, further work is needed before final dosage schedules can be established. The effectiveness of penicillin and streptomycin in gonorrhea has been adequately proved.

Chloromycetin has the advantage over aureomycin of being much less toxic, while aureomycin is probably more effective weight for weight. Therefore, it appears to us that their combined use may produce even more desirable results. Both antibiotics have an advantage over penicillin in that they are highly effective orally.

With the demonstration of the effectiveness of these two antibiotics in gonorrhea, our medical armamentarium against this disease is further strengthened. Under certain circumstances oral medication has its advantages.

Fusospirochetosis *

All of the antibiotics mentioned above are of some value in ridding the tissues of fusospirochetes. Particularly in granuloma inguinale is it necessary to treat these frequent secondary invading organisms in order to hasten healing of the specific lesion. Fusospirochetes found in approximately 21 percent of the patients having granuloma inguinale (14). They disappear slowly from the lesions of patients under treatment with streptomycin, aureomycin, and chloromycetin. Penicillin, however, is by far the most effective agent in ridding the patient of fusospirochetal organisms.

Streptomycin

Severe toxic reactions to streptomycin have been reported; however, these are more frequent in diseases requiring prolonged administration. In the first 100 cases of granuloma inguinale treated at the University of Georgia (12), 3 patients developed pruritus, another a generalized urticaria and circumoral vesicular eruption, and still another experienced burning sensations in the eye. These conditions were controlled by the administration of diphenhydramine hydrochloride, and all patients were able to complete therapy.

Aureomycin

The side effects from aureomycin, while uncomfortable, have not been serious. Some degree of nausea occurred in over 50 percent of the patients, and this was further complicated by vomiting and diarrhea in many. However, in only 2 of 73 cases was it necessary to discontinue the use of the drug because of persistent vomiting. Vomiting can usually be controlled, and the patient may complete therapy by reducing the daily dose.

Chloromycetin

Toxic manifestations are almost absent during the administration of chloromycetin. Only 3 patients in the group of 45 complained of nausea. A fourth developed a pharyngitis with multiple small ulcers in the throat; these cleared when chloromycetin was temporarily discontinued but recurred when treatment with the drug was resumed. However, with the aid of diphenhydramine hydrochloride, the patient was able to complete a course of treatment. The temperature and complete blood count remained normal throughout the episode. This is not a proved toxic reaction but is mentioned because we have heard of a similar occurrence in a patient treated with chloromycetin. It deserves further evaluation.

Conclusions

- 1. Penicillin is of value in the treatment of syphilis, gonorrhea, and fusospirochetosis. It is of little value in granuloma inguinale, lymphogranuloma venereum, or chancroid.
- 2. Streptomycin is effective in the treatment of granuloma inguinale. The minimum effective dose is considered to be 20 gm. in a period of 5 days. When this dose was employed in 92 of 142 cases treated by us, a cure rate of about 90 percent was obtained. However, 5 streptomycin-resistant cases were encountered. Streptomycin is also of value in the treatment of chancroid, gonorrhea, and fusospirochetosis, but not in the therapy of lymphogranuloma venereum.
- 3. Forty-seven patients having granuloma inguinale have been cured with aureomycin therapy. The two relapses that occurred have been effectively retreated with aureomycin, and both have remained well. No aureomycin-resistant cases have been encountered. The minimum total dose appears to be 20 to 25 gm. in 10 to 12.5 days; however, larger doses are required in patients having extensive lesions or showing some refractoriness to healing.

- 4. Chloromycetin is effective in the treatment of granuloma inguinale. Thirty-four patients with this disease have now been treated. The lesions in two patients relapsed at 2.5 months. Both were effectively re-treated with chloromycetin. No resistant cases have been seen. The minimum curative dose appears to be 20 to 25 gm.
- 5. Aureomycin therapy is of more value in the treatment of patients having late manifestations of lymphogranuloma venereum than in those with primary lesions and buboes.² Proctitis and inflammatory rectal strictures respond well to prolonged treatment with aureomycin, 50 to 100 gm. being necessary in some patients.
- 6. Chloromycetin is less effective than aureomycin in the treatment of lymphogranuloma venereum, and it is apparent from our small series of cases that aureomycin is the drug of choice in this disease.
- 7. Chancroid responds well to small doses of aureomycin, streptomycin, or chloromycetin,
- 8. Fusospirochetosis responds well to penicillin and slowly to streptomycin, aureomycin, or chloromycetin.
- 9. Gonorrhea may be effectively treated by penicillin, streptomycin, aureomycin, or chloromycetin.

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² A difference as great could happen once out of five times due to chance.

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The Control of Congenital Syphilis: Prevention and Case Finding

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Many times since the founding of this Nation we have waged wars and battled in many ways to preserve the life, freedom, and equality of our people. We have waged wars against aggression, against want, against prejudice, against disease, and against many other things in the interest of our fellow man.

In 1936, led by Dr. Parran, we began a real fight to bring syphilis under control and to prevent its ravages on mankind. With the advent of penicillin in 1943, we rolled up our sleeves, brought out our heavy guns, enlisted our "shock troops," and actually started fighting with an ever-increasing intensity.

Our fight against syphilis has had two main spearheads: first, the location and treatment of primary and secondary (early infectious) cases of syphilis; secondly, the location and treatment of infected contacts of primary and secondary syphilis patients. With the introduction of penicillin treatment, we opened (and have steadily increased) our third spearhead—the elimination of our backlog of previously unknown and untreated cases of latent and late latent syphilis. However, with eyes focused and forces concentrated on these three spearheads, we failed to take sufficient cognizance of the fact that the enemy was carrying on, with little hindrance, deadly undercover activities on a fourth front. Earlier this year, when figures compiled by the United States Public Health Service seemed definitely to indicate a decline in the incidence of primary and secondary syphilis, some of us began to smile and to relax somewhat. "The tide has turned," we thought. Our complacency, however, was short-lived for it was quickly pointed out,

from figures collected at the same time, that the incidence of congenital syphilis has remained constant for the past 5½ years—or, at least the morbidity reporting so indicates.

Dr. Bauer, in his editorial (1) in the September issue of The Journal of Venereal Disease Information, states that there has been a continuous decrease of infant mortality due to syphilis for the past 11 years. This would indicate that there should also have been a decline in the incidence of congenital syphilis.

We believe that there has been a decrease in the incidence of congenital syphilis in Georgia brought about by intensive case finding, reducing the prevalence of syphilis in the general population and among pregnant women. We therefore believe that if we will continue our educational and preventive measures and intensify our case-finding programs to eliminate the backlog of congenital syphilis cases now existing, we will see a dramatic drop in the number of cases of congenital syphilis reported in the next 12 to 24 months.

To indicate that the finding of cases of congenital syphilis can be improved in some places, at least—we would like to report the following: During the first 6 months of 1948, 11 communicable disease investigators in the field, instructed to find cases of primary and secondary syphilis, uncovered 10 cases of congenital syphilis. In the same 6-month period of 1949, after we had increased our efforts to find congenital syphilis cases, 22 investigators, or twice the former number, uncovered 380, or 38 times as many cases. This was accomplished without detracting from the effectiveness of the other phases of the work of the investigators; in fact, production in every phase of their work was quadrupled or better (2).

We believe that the measures and methods we are now using or plan to use in finding and preventing congenital syphilis in Georgia will be of general interest. Since approximately 93 percent of the cases of congenital syphilis reported in the last $2\frac{1}{2}$ years in Georgia were among Negro children (3), we are attempting to

secure a serologic test for syphilis on every pupil in the Negro schools during this school term. As a continuing program, every new pupil under 10 years of age will be tested. In this connection, we have worked out plans with the Department of Education, through our Joint Committee on Health and Education, so that school superintendents, supervisors, and teachers will know about the program and will be properly indoctrinated. der this program, we hope to see that no child is "set apart" or stigmatized because of a condition for which he is not responsible and to see that special study plans are made so that no child will be penalized for missing a few days from school while under treatment. The educational forces have been found to be most cooperative.

We are undertaking the completion of diagnostic observations on (1) every member of the family of any child treated for syphilis, a procedure enough of which has not been done previously; and (2) all children of syphilitic women referred to us for treatment, especially women with latent syphilis referred to us during the child-bearing age.

A number of rapid treatment center medical officers have reported that we receive into our rapid treatment centers many women in the seventh, eighth, and even the ninth month of pregnancy, who have primary or secondary syphilis. During a recent study (3), preliminary figures indicated that 53 percent of the pregnant women treated at Georgia rapid treatment centers were admitted with infectious syphilis, but that less than 27 percent of these received treatment within the first 4 months of pregnancy. For this reason, we have requested our prenatal clinics to adopt a policy of making a serologic test for syphilis at the time the patient is admitted to the clinic and at the eighth month of pregnancy. We hope that a program of physician information will induce private physicians to do likewise

We are at present initiating a program to give more widespread information about the Georgia prenatal blood-test law. Since Georgia has now adopted the dual form of reporting births, we are contemplating requesting legislative action to require the results of serologic tests to be shown on the confidential medical record (now prohibited). Follow-up could then be initiated from this information. It is felt that most of the physicians of the State would cooperate in such a program.

Here in Georgia, we are advising our staff that in the event of a choice between using their limited time for the follow-up of treated pregnancy cases or for casefinding activities, the time should be given to the latter. In the recent above-mentioned study (3), we followed more than 400 cases of pregnancy treated at rapid treatment centers in Georgia. Preliminary figures indicate that 85.4 percent of these cases had normal or sustaining outcomes. While we were unable to secure satisfactory data as to the reason for the fatal outcomes in these particular cases, our data do show that in 705 previous outcomes for these women, there were 77.6 percent live births and 22.4 percent fatal outcomes. In the confirmed outcomes of 308 cases, 97.1 percent were not infected and 2.9 percent were infected. As criteria for noninfection, we used the absence of clinical symptoms and a negative serologic test at the age of 3 months or older. Although the rate of infected infants in this study seems somewhat higher than that reported in the literature, we feel that as more cases are added, the rate will level off to about the same as that reported by Dr. Evan Thomas and others.

Surely all will agree that the biggest bulwarks behind which our enemy hides are superstition, fear, and ignorance. We firmly believe that our biggest and best weapon against syphilis—at least here in Georgia—is education. We have ini tiated a program which calls for the utili zation of every type of public education and information that is available. W believe that if we can overcome ignorance fear and superstition will also be con quered. The accomplishment of this wil require our best insight and planning and the use of the mediums most suited to place, time, and people. An example of this is seen in a report of one of our com municable disease investigators, who drove his automobile, on which was mounted a public address system, into the middle of a small Negro village concen trated around a turpentine still in the piny woods of south Georgia. By playing a little "boogie woogie" and giving ou some persuasive information, he was able to collect 71 blood specimens in about an hour from people who would probably never report to a doctor or clinic fo examination.

In summary, the control of congenitary syphilis in Georgia presents us with a choice of alternatives: Are we going to awaken ourselves to the moral challenge being made to our foresight, intelligence and compassion for our fellow man; our are we going to remain inert, destroying for him the hope of freedom from blind ness, insanity, and the loss of economic security because of a disease for which we know the prevention and cure?

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CURRENT NOTES AND REPORTS

WHO VD Teams in Field

The World Health Organization has a venereal disease team in India demonstrating modern technics of control, especially penicillin therapy for syphilis, reports the WHO Newsletter. Another VD team is preparing to go to Egypt, and still a third is planned for Haiti. In the Philippines a WHO venereal disease expert has spent 6 months helping to organize a venereal disease control program.

In Europe, WHO is participating with the International Children's Emergency Fund in over-all venereal disease control programs in Poland, Czechoslovakia, Bulgaria, Yugoslavia, Hungary, Italy, and Finland.

The Second World Health Assembly approved a program laying great stress on the importance of venereal disease control schemes to be started in underdeveloped areas, in addition to the programs already under way in Europe.

During debate, it was stated that in underdeveloped countries, the infant mortality rates from syphilis sometimes rise higher than 10 percent.

"Ignorant Cowboy" Enters the Comics

"Lucky Fights It Through" is the latest addition to the comic book attack on VD. It tells the story of Lucky Jordan, a cowboy who was led back to health and a "walk into the sunset" by hearing the range hands sing "That Ignorant, Ignorant Cowboy." Produced by Educational Comics, Inc., this comic book may be purchased from Communication Materials Center, Columbia University Press.

CURRENT LITERATURE

Note: Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 25 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

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A note on the clinical effectiveness of the newer antibiotics. A. M. Rutenburg, F. Schwemburg and J. Fine. 8: 111-113, July-Aug. 1949.

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- *Studies on the cultivation of *Treponema* pallidum. Ruth A. Boak, Margarette L. Fawcett and Charles M. Carpenter. 33: 409–415, Sept. 1949.
- *Studies on the effect of aureomycin on Treponema pallidum. Richter H. Wiggall, Harold E. C. Zheutlin, E. Randolph Trice, DuMont F. Elmendorf, Jr. and R. C. V. Robinson. 33: 416–423, Sept. 1949.
- *Speculations on the role of spreading factor (hyaluronidase) in experimental and human syphilis. Virgil Scott. 33: 424–428, Sept. 1949.
- *Abortive treatment of syphilis. Results obtained in the incubation, primary, and secondary stages of syphilis. Lee J. Alexander, Arthur G. Schoch and Walter B. Mantooth. 33: 429-436, Sept. 1949.
- Delayed administration of oral penicillin as prophylaxis for gonorrhea. V. W. H. Campbell, W. J. Dougherty and C. E. Curtis. 33:437-443, Sept. 1949.
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Studies on the cultivation of *Treponema pallidum*. Ruth A. Boak, Margarette L. Fawcett and Charles M. Carpenter. Am. J. Syph., Gonor. & Ven. Dis., 33: 409–415, Sept. 1949.

Motile spirochetes morphologically characteristic of *Treponema pallidum*

were observed from 34 to 97 days in original cultures made from syphilomas in 21 rabbits. The culture medium used was Brewer's modified thioglycollate medium supplemented with 10 percent inactivated goose or beef serum.

In 15 instances, the observations were carried out with the Nichols strain Others were identified as Ami, Fan, Est Rei, and 2 from Tho. Motile spirochetes were seen in the original culture (Nichols) for 84 days, in a first subculture for 87 days, in a second subculture for 23 days, and in a third subculture for 13 days.

On the basis of motile spirochetes betaine, citrulline, creatinine and dl ornithine were from 5 to 10 times more effective as supplements to the basal me dium than any of the other substances tested.

The presence in cultures of motile spirochetes morphologically like T. pallidum and isolated from syphilomas in rabbits produced by six strains is indicative that they were T. pallidum.

Studies on the effect of aureomycin of *Treponema pallidum*. Richter H. Wig gall, Harold E. C. Zheutlin, E. Randolph Trice, DuMont F. Elmendorf, Jr., and R. C. V. Robinson. Am. J. Syph., Gonor. & Ven. Dis., 33: 416–423, Sept. 1949.

Aureomycin was administered every a hours intramuscularly in three equal doses to rabbits in which syphilomas were caused by inoculation. Total dos ages used were 50, 100, and 200 mg. per kilogram. Five rabbits were used for each series. The treponemes in fully developed syphilomas remained relatively unchanged for a period of 5 days in the untreated rabbits. The composite curve of average treponeme counts from five rabbits showed a constant level.

No appreciable decrease in the number of treponemes was observed in the first 24 hours when 50 mg. of aureomycin per kilogram were given. At 48 hours there was a decrease of from 50 to 90 percent. There were darkfield-negative lesions and a marked decrease in the number of treponemes at 72 hours. In 96 hours only at

occasional lesion was darkfield positive.

Larger doses of aureomycin (100 and 200 mg. per kilogram) did not affect the rate of the disappearance of treponemes.

Treatment with aureomycin resulted in a concurrent decrease in the size of the lesions.

Another method used in this study was the protection test (prophylactic). Thirty rabbits, 50 percent of them being used as controls, were inoculated with *Treponema pallidum*. Within 5 minutes, 5 were treated with 12.5 mg. per kilogram of aureomycin, 5 with 25 mg. per kilogram of aureomycin, and 5 with 50 mg. per kilogram. These doses were repeated twice daily for 8 to 10 days. None of the animals receiving aureomycin developed orchitis or other evidence of syphilis.

In an observation on the effect of aureomycin in human syphilis, 15 patients with syphilis admitted to the Baltimore Rapid Treatment Center were given aureomycin. Each patient had darkfield-positive lesions. Aureomycin hydrochloride (250 mg. capsule) was given every 6 hours orally. The individual dose ranged from A darkfield was done 0.5 gm. to 1.0 gm. on each patient every day. The first 9 patients received 2 to 4 gm. of aureomycin per day for 2 days. At 24 hours the darkfield was still positive, and the number of treponemes had not decreased : at 48 hours 5 of the 9 patients were darkfield positive, but in each instance only one or two T. pallidum in each 50 fields were found.

Six patients given 4 gm, of aureomycin per day for 6 days became darkfield negative in 72 hours. Two patients were completely healed in 6 days.

At the end of the study period all 15 patients received 4.8 million units of penicillin.

The toxicity of aureomycin in rabbits included anorexia, diarrhea, and death which was higher than expected. In humans only diarrhea and nausea without vomiting were the reactions observed.

Speculations on the role of spreading factor (hyaluronidase) in experimental and human syphilis. Virgil Scott. Am.

J. Syph., Gonor, & Ven. Dis., 33: 424–428 Sept. 1949.

Evidence already available suggests that hyaluronidase may be of importance in syphilis.

It is agreed that syphilis is more severe in males than in females. A possible explanation for this sex difference is hyaluronidase, males having a richer source for this substance in the testes.

The testis is the most favorable site for inoculation. It is more favorable than the skin. Abortive and curative treatment doses of penicillin were two to four times greater in animals inoculated into the testes than in those inoculated into the skin.

Syphilis is milder in castrated than in normal males. Estrogens suppress spermatogenic action, and testes so affected offered increased resistance to the *Treponema pallidum*.

Granulating wounds and other types of inflammatory tissues react to syphilitic infection by giving off a growth-promoting factor of tissue, which may be hyalurouidase. This may offer a medium for the growth of *T. pallidum*.

In interstitial keratitis, the spreading factor may be related to the hyaluronic acid ester of the cornea. Puberty is the time of highest incidence. Testicular extract may be concerned. Perhaps the combination of *T. pallidum* and hyaluronidase may be concerned with the pathogenesis of interstitial keratitis.

It is possible that the affinity of *T. pallidum* for certain tissues may be, at least in part, related to the type of supporting ground substance and its permeability as affected by hyaluronidase produced by the host or the spirochete itself.

Abortive treatment of syphilis. Results obtained in the incubation, primary, and secondary stages of syphilis. Lee J. Alexander, Arthur G. Schoch and Walter B. Mantooth. Am. J. Syph., Gonor. & Ven. Dis., 33: 429–436, Sept. 1949.

This is a report on almost 3 years of experience with the treatment, during the incubation stage, of persons who were exposed to darkfield-positive primary and secondary syphilis.

During the first 20 months of this study, 148 persons who had been in contact with patients having darkfield-positive primary and secondary syphilis were given abortive treatment consisting of 900,000 units of calcium penicillin in oil and beeswax, 3 cc. of bismuth ethylcamphorate, and 0.05 to 0.06 gm. of arsenoxide. During the following year, 108 persons who had been in contact with patients having primary and secondary syphilis received a modified abortive treatment, the arsenoxide being omitted from the former treatment formula.

Of the 256 persons who received the abortive treatment, 13 eventually showed evidence of early syphilis, one a second time. The evidence in these 14 infections supports the diagnosis of reinfection.

A control group consisted of 161 persons who were in contact with darkfield primary and secondary cases of syphilis. These received no abortive treatment. One hundred (62.1 percent) of these acquired early syphilis.

Of the contacts who returned 1 week after receiving abortive treatment, 10.2 percent showed a "provocative effect."

The preliminary results in patients with primary and secondary syphilis who were treated with the abortive treatment schedule are good.

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Oral administration of aureomycin in the treatment of gonorrhea. Calvin H. Chen, Robert B. Dienst and Robert B. Greenblatt. Urol. & Cutan. Rev., 53:394– 397, July 1949.

Aureomycin is the first antibiotic to be effective against all five venereal diseases.

Since the drug could be easily tolerated, the authors administered higher dosages of aureomycin than the usual, and the results were compared with penicillin therapy. Twenty cases in the study received aureomycin treatment for gonorrhea. One gm. 3 times a day after meals for 2 days was the treatment schedule. The toxicity consisted of some slight nauseation and one case of vomiting. Twenty other patients with gonorrhea received an intramuscular injection of 300,000 units penicillin G in oil and wax.

All patients given aureomycin were cured. Two of twenty patients treated with penicillin failed to recover. This was a 90-percent cure with penicillin therapy and a 100-percent cure with aureomycin therapy. Aureomycin later cured the 2 penicillin failures.

The case of a 27-year-old male with a urethral discharge is included. He received 6,000,000 units penicillin for the disorder but no cure resulted. This lasted for 5 months. He was placed on a 2-day aureomycin schedule. He reported back after 2 days that the discharge had disappeared after the first dose of the antibiotic. The only drug reaction was some itching. No gonococci could be demonstrated.

Aureomycin eventually may be used as a prophylaxis for all venereal diseases. It is convenient to take orally, and its cure rate is high.

STATISTICS

Diagnostic Observations ^a for Venereal Disease Completed by State and Territorial Health Departments, Fiseal Year 1949

Area	Estimated eivilian population	Observa- tions	Number com- pleted	cases d	yphilis liagnosed admitted es	Ohservations completed per new syphilis case diagnosed		
	in thousands	eom- pleted ^b	per 1,000 popula- tion	Allstages	Primary or sec- ondary	All stages	Primary or sec- ondary	
Region 1—Total Connecticut Maine Massachusetts New Hampshire Rhode Island Vermont •	9, 113 1, 970 884 4, 623 531 740 365	8, 230 2, 363 594 4, 770 51 452 0	0. 9 1. 2 0. 7 1. 0 0. 1 0. 6	1, 676 355 158 974 6 183 0	376 77 57 178 4 60	4. 9 6. 7 3. 8 4. 9 8. 5 2. 5	21. 9 30. 7 10. 4 26. 8 12. 8 7. 5	
Region 2—Total Delaware New Jersey New York New York City Pennsylvania Philadelphia Pittsburgh	29, 510 290 4, 582 14, 140 9, 251 10, 498 3, 373 2, 100	177, 433 3, 679 55, 795 76, 051 64, 324 41, 908 30, 721 3, 431	6. 0 12. 7 12. 2 5. 4 7. 0 4. 0 9. 1 1. 6	17, 540 467 3, 003 7, 540 5, 454 6, 530 3, 947 667	3. 839 97 566 1, 868 1, 231 1, 308 712 205	10. 1 7. 9 18. 6 10. 1 11. 8 6. 4 7. 8 5. 1	46. 2 37. 9 98. 6 40. 7 52. 3 32. 0 43. 1 16. 7	
Region 3—Total District of Columbia Maryland Baltimore North Carolina Virginia West Virginia	11, 439 831 2, 111 1, 306 3, 660 2, 955 1, 882	212, 532 27, 795 25, 260 12, 602 103, 766 31, 153 24, 558	18. 6 33. 4 12. 0 9. 6 28. 4 10. 5 13. 0	14, 677 1, 750 3, 597 2, 093 6, 065 2, 215 1, 050	5, 165 587 1, 145 686 2, 255 781 397	14. 5 15. 9 7. 0 6. 0 17. 1 14. 1 23. 4	41. 1 47. 4 22. 1 18. 4 46. 0 39. 9 61. 9	
Region 4—Total Kentucky Michigan Ohio	16, 487 2, 761 6, 059 7, 667	124, 788 43, 709 21, 516 56, 563	7. 6 15. 8 4. 0 7. 4	7, 892 2, 175 1, 956 3, 761	2, 182 759 639 784	15. 8 20. 1 12. 5 15. 0	57. 2 57. 6 38. 4 72. 1	
Region 5—Total	18, 331 8, 364 4, 645 3, 833 2, 888 3, 246	90, 026 64, 793 57, 881 11, 579 10, 796 2, 858	4. 9 7. 7 12. 5 3. 0 3. 7 0. 9	4, 412 2, 961 2, 094 1, 120 129 202	$1,447 \\ 999 \\ 661 \\ 353 \\ 19 \\ 76$	20. 4 21. 9 27. 6 10. 3 83. 7 14. 1	62, 2 64, 9 87, 6 32, 8 568, 2 37, 6	
Region 6—Total. Alabama Florida. Georgia Mississippi. South Carolina Tennessec. Puerto Rieo Virgin Islands.	17, 388 2, 827 2, 280 3, 114 2, 087 1, 929 3, 086 2, 039 26	1, 124, 640 243, 966 145, 059 285, 709 141, 662 80, 811 54, 203 165, 613 7, 617	64. 7 86. 3 63. 6 91. 7 67. 9 41. 9 17. 6 81. 2 293. 0	51, 675 6, 004 6, 817 10, 445 12, 093 4, 598 4, 164 7, 399 155	10, 544 811 1, 800 2, 536 1, 946 1, 379 1, 426 620 26	21. 8 40. 6 21. 3 27. 4 11. 7 17. 6 13. 0 22. 4 49. 1	106. 7 300. 8 80. 6 112. 7 72. 8 58. 6 38. 0 267. 1 293. 0	
Region 7—Total	10, 802 2, 590 1, 913 3, 901 1, 584 1, 282 541 575	40. 726 1, 203 9, 106 21, 090 12, 141 5, 496 0 3, 831	3. 8 0. 5 4. 8 5. 4 7. 7 4. 3 0 6. 7	3, 262 187 779 2, 136 1, 130 101 0 59	$777 \\ 81 \\ 134 \\ 517 \\ 220 \\ 26 \\ 0 \\ 19$	$ \begin{array}{c} 12.5 \\ 6.4 \\ 11.7 \\ 9.9 \\ 10.7 \\ 54.4 \\ -64.9 \end{array} $	52. 4 14. 9 68. 0 40. 8 55. 2 211. 4 201. 6	
Region 8—Total Arkansas Louisiana New Mexico Oklahoma Texas	14, 290 1, 912 2, 535 538 2, 275 7, 030	383, 704 151, 034 45, 374 4, 013 45, 265 138, 018	26, 9 79, 0 17, 9 7, 5 19, 9 19, 6	21, 673 5, 714 5, 594 237 1, 547 8, 581	$4,328 \\ 583 \\ 1,171 \\ 37 \\ 574 \\ 1,963$	17. 7 26. 4 8. 1 16. 9 20. 3 16. 1	88. 7 259. 1 38. 7 108. 5 78. 9 70. 3	
Region 9—Total Colorado Idaho Montana Utah Wyoming	3, 037 1, 127 525 487 638 260	14, 473 3, 407 7, 719 654 1, 920 773	4. 8 3. 0 14. 7 1. 3 3. 0 3. 0	564 358 73 23 88 22	$\begin{array}{c} 152 \\ 110 \\ 12 \\ 9 \\ 17 \\ 4 \\ \end{array}$	25. 7 9. 5 105. 7 28. 4 21. 8 35. 1	$\begin{array}{c} 95.2 \\ 31.0 \\ 643.2 \\ 72.7 \\ 112.9 \\ 193.2 \end{array}$	

Diagnostic Observations ^a for Venereal Disease Completed by State and Territorial Health Departments, Fiscal Year 1949—Continued

Area	Estimated civilian population	Observa- tions	Number eom- pleted per 1,000	eases	y philis diagnosed admitted es	pleted	ions eom- per new s ease di- l
	in thousands	pleted b	popula- tion	All stages	Primary or see- ondary	All stages	Primary or sec- ondary
Region 10—Total	1, 544	100, 423 9, 872 58, 847 1, 678 4, 952 21, 483 0 3, 591	6. 8 15. 5 6. 1 12. 1 3. 2 9. 3 8. 7	6, 550 510 4, 821 67 315 693 0 144	1, 855 175 1, 272 22 144 236 0	15. 3 19. 4 12. 2 25. 0 15. 7 31. 0	54. 1 56. 4 46. 3 76. 3 34. 4 91. 0 598. 5
Total continental United States	142, 659	2, 100, 154	14.7	122, 223	30, 013	17. 2	70. 0
'Total United States includ- ing Territories	145, 139	2, 276, 975	15. 7	129, 921	30, 665	17. 5	74. 3

<sup>An examination of a person to determine the presence or absence of venereal disease other than observations to determine response to therapy.
Excluding observations dropped or transferred.
No public venereal disease clinics.
- Data are unknown.
Rate not calculable, base is zero or unknown.</sup>

Source: Bureau of the Census population reports: States—Series P-25, No. 12, July 1947; Cities-Series P-21, Nos. 8, 12, 15, 25, 28, 29, April 1947; Territories—Series P-46 No. 9, July 1945. Observation and diagnosed ease data from P. H. S. Form 8954-A. FSA-PHS Division of Venereal Disease, Office of Statistics. 12/13/49 (A. S./M. L.)



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FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

52.9

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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Editor: THEODORE J. BAUER, Medical Director Chief, Division of Venereal Disease

The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription Price: Domestic, 75 cents a year; Foreign, \$1.15

Rapid Treatment of Early Syphilis: Progress Report—June 1949¹

Theodore J. Bauer, Medical Director, Lida J. Usilton, Public Health Administrator, and Eleanor V. Price, Biostatistician, United States Public Health Service

Since 1943, the United States Public Health Service, in cooperation with 50 State and locally sponsored rapid treatment centers, has conducted an evaluation of the effectiveness of various schedules of treatment for early syphilis. Schedules employed during this period have included massive arsenotherapy, fever therapy, and penicillin.

The present report, the twelfth in a continuing series, is limited to schedules utilizing penicillin (either alone or in conjunction with other antisyphilitic therapy) which have been reported to the statistical section of the Division of Venereal Disease. The statistical method employed in this evaluation (1) is based on the assumption that cases which lapse from observation will have the same experience as those which remain under observation.

The first analysis is based on the records of 5,400 patients treated solely with crystalline penicillin G, administered in aqueous solution or peanut oil and beeswax, with total dosages ranging from 2,400,000 units to 18,000,000 units. All patients were previously untreated for syphilis. Of the total number, 1,401 patients were observed for a minimum of 21 months following treatment. Diagnosis at time of treatment was seronegative primary syphilis in 211 patients, seropositive primary syphilis in 348, and secondary syphilis in 842. Seronegativity rates at the 21- to 24-month observation period for these three stages of infectious syphilis are 90.0, 85.9, and 78.7 percent, respectively; cumulative re-treatment rates are 10.0, 12.2, and 15.6 percent. Because of the difficulty of differentiating between reinfection and relapse, reinfections as well as relapses have been included in the re-treatment rates. When cases diagnosed as probable reinfections are omitted, the differences between the results in these three stages of syphilis are much greater. Cumulative rates for serologic failure or clinical relapse are 2.3 percent for seronegative primary syphilis, 6.2 percent for seropositive primary syphilis, and 12.0 percent for secondary syphilis (chart 1).

Table 1 presents 45 schedules of therapy in which a minimum of 20 patients with secondary syphilis have been observed for at least 21 months following treatment. The results for the three early infectious stages of syphilis are presented separately, since re-treatment rates vary according to the stage of syphilis at the time treatment is instituted, and because of the fact that proportionately the same number of primary and secondary cases were not treated with each sched-The 45 schedules, which have been divided into two groups (those employing crystalline penicillin G and those employing amorphous penicillin), have been listed from the highest to the lowest rate of seronegativity in the secondary stage at the 21- to 24-month observation period Amorphous penicillin, which (table 1). was used from 1943 to July 1946, varied constantly in relative proportions of fractions G, F, X, and K and in potency in units per milligram. As a result, the amorphous penicillin schedules are of little value in determining the effectiveness of penicillin in the treatment of syphilis. They are presented here for the last time, not only for the record, but to illustrate the reason for the divergence of opinion as to the effectiveness of penicillin in the treatment of syphilis. These schedules vary in rate of seronegativity from 88.0 percent to 38.2 percent and in re-treatment rate from 6.6 percent to 61.8 percent in the secondary stage.

¹ From the Division of Venereal Disease.

Table 1.—Results of 45 schedules of penicillin therapy 21 to 24 months following treatment for primary and secondary syphilis

[Includes only schedules with a minimum of 20 cases of secondary syphilis observed for at least 21 months following treatment]

Seronegative primary Seropositive primary	Sero	Seronegative primary	ary	Ser	Seropositive primary	ary		Secondary	
Schedule of therapy	Cases observed 21-24 months	Cumulative percent re-tr ea ted	Percent sero- negative	Cases observed 21–24 months	Cumulative percent re-treated	Percent sero- negative	Cases observed 21–24 months	Cumulative percent re-treated	Percent sero- negative
Crystalline G: 4,800,000 u., 80,000 every 3 hrs. 4,800,000 u., 25,000 every 3 hrs. 2,800,000 u., 25,000 every 3 hrs. 2,400,000 u., 40,000 every 3 hrs. 2,800,000 u., 25,000 every 2 hrs. 2,400,000 u., 25,000 every 2 hrs. 2,400,000 u., 25,000 every 2 hrs. 2,800,000 u., 25,000 every 3 hrs. 2,800,000 u., 25,000 every 3 hrs. 2,800,000 u. POB, 300,000 every 24 hrs. 1,800,000 u., 16,967 every 2 hrs.+5 arsenoxide and 3 bismuth.	25 6 8 1 1 8 8 8 2 8 8 8 8 8 8 8 8 8 8 8 8 8	$\begin{array}{c} 13.2(\pm 15.1)\\ 16.4(\pm 10.5)\\ 16.9\\ 7.8(\pm 8.7)\\ 16.7\\ 9.0(\pm 9.8)\\ 11.3(\pm 12.4)\\ 0.0\\ 18.0(\pm 11.1)\\ \end{array}$	88.22 92.6 92.22 92.22 100.0 81.9	38 38 39 12 11 12	$\begin{array}{c} 13.6 (\pm 14.3) \\ 15.1 (\pm 11.9) \\ 10.2 \\ 16.8 (\pm 10.0) \\ 11.2 \\ 11.1 (\pm 8.3) \\ 11.1 (\pm 8.3) \\ 11.2 (\pm 11.4) \\ 18.2 \\ 16.8 (\pm 7.1) \\ 16.8 (\pm 7.1) \end{array}$	988848888 9998848888 1888888888	104 110 176 138 24 105 109 386	13.8 (±6.8) 13.5 (±5.9) 13.5 (±7.8) 16.6 (±6.3) 20.0 (±16.3) 14.4 (±6.8) 22.8 (±8.9) 9.5 (±13.1)	4.8.8.8.8.8.6.1.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0
Amorphous: 1,200,000 u, 20,000 every 3 hrs.+3 sessions of fever 1,200,000 u, 40,000 every 2 hrs. 4,200,000 u, POB, 300,000 every 24 hrs.+5 arsenoxide and 3 hismuth 5,000,000 u, POB, 500,000 every 24 hrs. 2,400,000 u, 40,000 every 3 hrs.+8 arsenoxide and 3 hismuth 9,600,000 u, POB, 800,000 every 24 hrs. 4,800,000 u, POB, 300,000 every 24 hrs. 2,400,000 u, POB, 300,000 every 3 hrs.+8 sessions of fever 2,400,000 u, POB, 900,000 every 3 hrs.+8 sessions of ever	8 4 8 4 8 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6	10.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	0.09 0.00 0.00 0.00 0.00 0.00 0.00 0.00	4111 112 112 122 124 125 126 126 126 126 126 126 126 126 126 126	27. 8.7. 8.5.0 16.5.1 16.0 16.0 16.0 16.0	7.28 99.59 7.20 100.88 99.50 9.50 9.50 9.50 9.50 9.50 9.50 9.5	28 108 23 88 28 65 85 85 85 85 85	12.0° 13.0°	8888 87.99.0 77.77.77 77.78.9 77.78.9 77.78.9 77.78.9 77.78.9
9,600,000 u. POB, 600,000 twice weekly. 1,200,000 u. 20,000 every 3 hrs.+8 arsenoxide. 4,200,000 u. POB, 300,000 every 24 hrs. 3,000,000 u. POB, 300,000 every 24 hrs. or 150,000 every 12 or 24 hrs. 1,200,000 u. POB, 300,000 every 24 hrs. or 150,000 every 12 or 24 hrs. 2,800,000 u. AOB and and an arrelation of the second of	10 448 144 123 333 33	2001 2001 2002 2003 2000 2000 1000 1000	25.77 20.77 20.77 20.09 20.09 20.09	128 14 14 31 52 16 16	27. 5 12. 5 12. 5 21. 9 21. 9 21. 9	でいる。 でいる。 でいる。 でいる。 でいる。 でいる。 でいる。 でいる。	20 373 47 103 181 181	44444444 044464444	725.3 722.3 70.7 70.7 70.2
1,560,000 u., 20,000 every 3 hrs. 2,400,000 u., 40,000 every 3 hrs. 1,200,000 u. in 28-30 hrs. 4 hrs. fever. 1,700,000 u., 20,000 every 3 hrs. 1,800,000 u., 16,667 every 2 hrs. 45 arsenoxide and 3 bismuth. 1,200,000 u., 40,000 every 6 hrs. 1,300,000 u., 20,000 every 6 hrs.	838 833 71 71	7.52.22.25. 7.52.25.25. 7.58.25.25.25.25.25.25.25.25.25.25.25.25.25.	92.3 84.6 1.1.3 8.6 1.1.3 1.2 1.3 1.3 1.3 1.3 1.3 1.3 1.3 1.3 1.3 1.3	100 100 128 138 138 138 138 138 138 138 138 138 13	18. 25. 28. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4.	7.07 60.08 60.8 7.08 6.49 6.49 6.49 6.49	218 218 62 170 170	38.85.85.8 20.13.86.92.0 20.13.86.9	6.55 6.45 6.45 6.45 6.55 6.55 6.55 6.55
1,200,000 u., 16,667 every 3 hrs.+5 arsenoxide. 2,400,000 u., 20,000 every 3 hrs. 2,700,000 u., 10,000 every 3 hrs. 1,600,000 u., 10,000 every 3 hrs. 1,600,000 u., 16,667 every 3 hrs. 1,200,000 u., 16,667 every 3 hrs. 2,400,000 u., 16,667 every 3 hrs. +5 arsenoxide and 3 bismuth. 2,400,000 u., 16,607 every 3 hrs. +6 arsenoxide and 3 bismuth. 2,400,000 u., 10,000 every 3 hrs. +8 arsenoxide and 3 bismuth. 3,000 every 3 hrs.+8 arsenoxide and 3 bismuth. 3,000 every 3 hrs.+8 arsenoxide and 3 bismuth.	8 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2,5% % % % % % % % % % % % % % % % % % %	601 601 6001 644 600 644 664 664 664 664 664 664 664	8 - 8 3 3 3 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	45.22.22.22.22.22.22.22.22.22.22.22.22.22	468777888888888888888888888888888888888	128 108 108 613 86 132 14 132 272 273	25.58.88.88.88.89.15.69.89.89.89.89.89.89.89.89.89.89.89.89.89	60 90 90 90 90 90 90 90 90 90 90 90 90 90
600,000 u. in 42 hrs.+8-10 hrs. fever. 10,000,000—25,000,000 u., intravenous drip.	24	24.3 29.9	70.2	16	24.5	56.7	23	61.8	43.0

CUMULATIVE RE-TREATMENT RATES FOLLOWING CRYSTALLINE PENICILLIN G (AQUEOUS OR POB) AND BASIS FOR RE-TREATMENT BY STAGE OF SYPHILIS

(21-24 MONTHS OBSERVATION PERIOD)

STAGE OF SYPHILIS	CASES OBSERVED	CUMULATIVE PERCENT RE-TREATED 0 5 10 15
SECONDARY	842	
SEROPOSITIVE PRIMARY	348	
SERONEGATIVE PRIMARY	211	

SEROLOGIC

FAILURE

In the 9 schedules shown in the first section of table 1, rates of seronegativity for schedules with a minimum of 20 cases vary from 65.3 percent to 84.4 percent for secondary syphilis. Cumulative retreatment rates for secondary syphilis vary from 9.5 percent to 22.8 percent. Retreatment rates in the secondary stage were slightly lower in the two 4,800,000unit schedules than in the two 2,400,000unit schedules (differences of 2.8 percent and 3.5 percent) and lower in the 2-hour than in the 3-hour interval schedules (differences of 2.2 percent and 2.9 percent). These differences, however, are not statistically significant.

Preliminary Results of Evaluation of Procaine Penicillin in Oil With 2 Percent Aluminum Monostearate

Widespread interest has been aroused in the treatment of syphilis with procaine penicillin. Of particular interest are the one-injection schedules utilizing procaine penicillin with 2 percent aluminum monostearate. It is felt, therefore, that the time is opportune for a preliminary report on the results of these schedules, although the period of posttreatment observation is still far too short for definite conclusions.

CLINICAL

RELAPSE

This evaluation, based on reports received through December 1949, includes the "Volunteer Study" cases of the Experimental Therapeutics Study Section which have been furnished through the courtesy of the Southwest Medical Foundation, Bellevue Hospital, the University of Pennsylvania, Washington University at St. Louis, Johns Hopkins University, Vanderbilt University, Columbia University, the University of Virginia, Emory University, and the Medical College of Alabama. The Division of Venereal Disease is indebted, also, to the Chicago Intensive Treatment Center, the Marine

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PROBABLE.

REINFECTION

Table 2,—Comparison of procaine penicillin with 2 percent aluminum monostearate and crystalline penicillin G in aqueous solution in the treatment of early syphilis

[Seronegative primary syphilis]

	re-treated	Sero- negative			92.3 100.0 100.0 100.0 100.0 100.0 100.0 100.0 100.0		or 7 days	90000000000000000000000000000000000000
	Percent not re-treated	Sero- positive		2,400,000 units	7.7		2,400,000 units—1,200,000 every 4 or	6.7
	Cumulative	re-treat- ment rate		2,400,00			000 units—1,2	
	1000 Foto	observed	1 injection		22 22 22 23 24 25 26 27 27 26 26 27 27 26 26 26 26 26 26 26 26 26 26 26 26 26	2 injections	2,400,	44444888222221 66847688
	re-treated	Sero- negative	nostearate—		96. 89.34 81.22 87.22 67.66 67.66 67.66 67.66	nostearate—	7 days	88. 100.0 100.0 100.0 100.0 100.0 100.0 100.0 100.0 100.0 100.0
[Seronegative primary syphilis]	Percent not re-treated	Sero- positive	uminum mo	0 units	3.6	uminum mo	00,000 every	11.1
	Cumu]ative	Sero- Sero- Percent not re-treated Total cases Sero- agative ment rate positive positive Procaine penicillin with 2 percent aluminum monostearate—1 injection		1.200,000 units	10. 10. 10. 10. 10. 10. 10. 10. 10. 10.	n with 2 percent aluminum mo 2,400,000 units—1,200,000 every	00 units—1,20	
egative prin		observed	enicillin with		282 222 222 222 222 232 248 248	Procaine penicillin with 2 percent aluminum monostearate—2 injections days 2,400,000 units—1,200,000 every 7 days 2,400	2,400,00	8888441101008884
[Seroi	re-treated	Sero- negative	Procaine p		97.2 100.0 100.0 100.0 100.0 100.0 100.0 100.0 100.0	,000 every 4	days	96. 100. 100. 100. 100. 100. 100. 100. 10
	Percent not re-treated	Sero- positive		units	0,00 000			7.%
	Cumulative	re-treat- ment rate		300,000 units			2,400,000 units—1,200	
		observed			112588888888888888888888888888888888888		2,400,00	22222222224
		Observation period	(HIOTE)		Less than 1. 1-2. 2-3. 2-3. 3-4. 3-4. 5-6. 6-7. 6-7. 8-9. 9-10. 11-12.			Less than 1 1-2s than 1 1-12

ł in aqueous solution	4,800,000 units—53,333 every 2 hours	43. 43. 43. 43. 44. 44. 44. 44.
Crystalline penicillin G in aqueous solution	2,400,000 units—26,667 every 2 hours	68 67 67 68 69 60 63 63 63 63 63 63 63 63 63 63
Procaine penicillin with 2 percent aluminum monostearate—4 injections	4,800,000 units—1,200,000 every 7 days	37 36 37 37 38 39 40 50 11.6 17.9 18 17.9
		Less than 1 1. Less than 1 2. 3 3. 4 4. 5 5. 6 6. 7 7. 8 9. 9 10. 11 11-12

2 Table 3.—Comparison of procaine penicillin with 2 percent aluminum monostearate and crystalline penicillin G in aqueous solution in the treatment of early syphilis

				Sord	positive prin	[Scropositive primary syphilis]						
	Tho for longon		Percent not re-treated	re-freated	Thofol oncom	Cumulative	Percent not re-treated	re-treated	Thefol secon	\sim	Percent not re-treated	re-treated
Observation period	observed	ro-troat- ment rate	Soro- positive	Sero- nogativo	observed	ro-tront- ment rate	Soro- positive	Sero- nogative	obsorved	ro-trent- ment rate	Sero- positive	Sero- negative
				Procaine p	enicillin wit	Precaine penicillin with 2 percent aluminum menostearate—1 injection	aminan no	nostourato	1 injection			
		300,000 units	mits			1,200,000 units) units			2,400,000 units) units	
Toss than 1 1-2 3-4 4-5 5-6 7-8 8-9 10-11	888888888888888888888888888888888888888	ය. කු කු කු කු කු කු කු කු කු ක ලා සා	2008 2008 2008 2008 2008 2008 2008 2008	43.3 6 66.7 7 75.2 2 75.2 2 76.2 2 81.5 2 81.5 5 81.5 5 81.5 6 81.5 6 81.5 6	48 42 42 42 42 43 40 13 13 12 13 12 13 12 13 14 14 15 16 17 17 17 17 17 17 17 17 17 17 17 17 17	43.3 48	97.9 68.8 68.8 68.8 30.0 22.2 20.8 18.0 18.0 16.7 17.2 17.2 10.8 10.0 10.0 10.0 10.0 10.0 10.0 10.0	2.1.3 31.3.1 65.1.4 65.2.9 66.9.2 66.9 67.7 70.5 67.7 70.5 68.2 70.5 86.2	42 42 40 36 38 32 32 27 22 20 18 14 7 7 7 7 7 2 18 18 18 18 22 22 27 27 27 27 27 27 27 27 27 27 27	0.000 0.000	95.2 66.7.2 7.2.5.1 2.2.6 2.1.0 9.1 9.1 6.0	4.8.7.8.9.7.8.8.9.9.8.8.9.9.8.8.8.9.9.9.9
	2,400,0	2,400,000 units—1,200,000 every 4 days	00,000 every 4	days	2,400,000 11	2,400,000 units—1,200,000 every 7 days	0 every 7 da;	V8	2,400,000 u	2,400,000 units-1,200,000 every 4 or 7 days	every 4 or 7	days
Tess than 1-2ss than 1-2ss than 1-2ss than 1-2ss than 1-2ss than 10-11 the same Information. March 1950	4688888888848758	% & & & & & & & & & & & & & & & & & & &	86477 & Q. C.	25.7.1.1.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2	752538888841 1111111111111111111111111111111	13.0 13.0 13.0 13.0 13.0 13.0 13.0	6.53 6.53 6.53 6.53 6.53 6.53 6.53 6.53	24.7 25.0 25.0 25.0 25.0 25.0 25.0 25.0 25.0	85 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	1.0.c. 1.	0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	0.4.2.2.4.4.5.8.8.8.8.8.8.8.8.9.1.0.0.4.0.4.0.8.8.8.8.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9

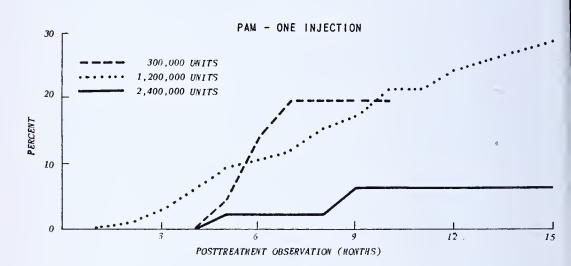
ous solution	4,800,000 units—53,333 every 2 hours	74
Crystalline penicillin G in aqueous solution	2,400,000 units—26,667 every 2 hours	110 110 110 107 108 108 109 109 109 109 109 109 109 109
Procaine penicillin with 2 percent aluminum monostearate—4 injections	4,800,000 units—1,200,000 every 7 days	48 48 4.3 4.3 4.3 4.3 4.3 4.3 4.3 4.3 4.3 4.3
		Less than 1 1-2 2-3 2-3 3-4 4-5 6-7 6-7 7-8 9-10 10-11 11-12

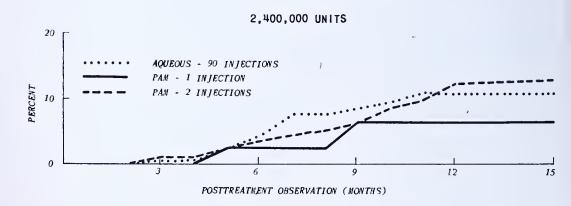
Table 4.—Comparison of procaine penicillin with 2 percent aluminum monostearate and crystalline penicillin G in aqueous solution in the treatment of early syphilis

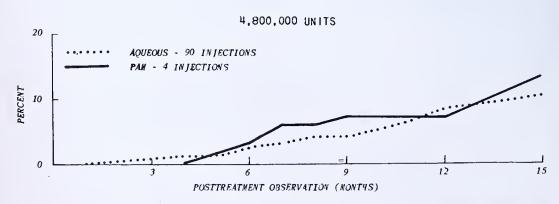
	Total pases C1				Less than 1 32 32 32 32 32 32 32 32 32 32 32 32 32	2,400,000	Less than 1													
	Cumulative	re-treat- ment rate															300,000	4.8.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.9.) units—1,20	00000000000000000000000000000000000000
		Sero- positive		300,000 units	0.00 0.00	Proc. 2,400,000 units—1,200,000 every 4 days	99999798888444 %99899994444 908999													
	Percent not re-treated	Sero- negativo Proeaine p	Proeaine p		3.1 16.1 16.1 16.1 16.1 16.1 16.1 16.1 1	4 days	- 1.0 % 4.0 % 7.2													
[Seeondary syphilis]	Totalogoga	observed	enieillin wit		119 119 109 87 867 67 67 61 48 48 48 48 48 48 48 48 48 48 48 48 48	2,400,(153 175 183 183 183 183 183 183 183 183 183 183													
syphilis	Cumulative	re-treat- ment rate	Procaine penicillin with 2 percent aluminum monostearate—1 injection	1,200,0	0.8 9.7 7 10.5 2 11.2 0 17.3 3 21.4 4 22.1.4	000 units—1,	9.4 w & & & & & & & & & & & & & & & & & &													
-		Sero- positive	luminum me	1,200,000 units	100.00 98.3 98.3 90.9 90.9 90.9 83.5 28.2 28.2 28.2 28.2 44.5 44.5 44.5 44.5 44.5 44.5 44.5 44	2,400,000 units—1,200,000 every 7 days	100 96.77 80.00 100.00													
	Pereent not re-treated	Sero- negative	nostearate-		119 0.8	7 days	8,12,2,2,4,4,4,6,5,6,6,6,6,6,6,6,6,6,6,6,6,6,6,6													
		observed	1 injection		62 62 60 60 60 60 83 83 83 83 83 83 83 83 83 83 83 83 83	2,400,	211 206 196 185 175 175 175 175 175 175 175 175 175 17													
	Cumulative	re-treat- ment rate		2,400,0	න්න්න්න්තිව් වේ වේ න්න්න්න්තිව් වේ වේ	2,400,000 units-1,200,000 every 4 or 7 days	Q . 94475% \Q \q													
		Sero- positive		2,400,000 units	0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	00,000 every	2.000 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0													
	Pereent not re-treated	Sero- negative			1.01 3.20 3.20 5.20 5.40 5.40 5.40 5.40 5.40 5.40 5.40 5.4	4 or 7 days	0.4.718.4.4.2.07.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.													

		41.0 6.2 6.2 6.2 6.2 6.2 6.3 6.3 6.3 6.3 6.3 6.3 6.3 6.3
	2,400,000 units—53,333 every 2 hours	99.6 97.6 97.7 97.1 97.1 98.2 98.4 98.2 98.2 11.0 11.0 11.0 11.0
solution	0 units—53,33	Q .4-998440000 4000011110000
Crystalline penielllin G in aqueous solution	2,400,00	24.2 24.2 24.2 22.2 22.1 22.1 20.0 20.0 20.0 192
	nırs	0.2.2.2.2.4.4.2.2.2.2.2.2.2.2.2.2.2.2.2.
	2,400,000 units—26,667 every 2 hours	99989988998999999999999999999999999999
		0 .00044706800111 0004470100000111
	2,400,00	222 222 208 208 208 191 191 171 171 162
ıminum	4,800,000 units—1,200,000 every 7 days	7.1.2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
2 percent alu 4 injections		89988888888888888888888888888888888888
Procaine penicillin with 3 monostearate—		1.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2
Procaine pe	4,800,000	25.1 15.0 15.0 15.0 15.0 15.0 15.0 15.0 1
	1	
		Less than 1 2 1-2 2-3 3-4 4-5 5-6 6-7 9-10 11-11

CUMULATIVE RE-TREATMENT RATES IN SECONDARY SYPHILIS FOLLOWING PROCAINE PENICILLIN WITH 2% ALUMINUM MONOSTEARATE (PAM) OR CRYSTALLINE PENICILLIN G IN AQUEOUS SOLUTION







Hospital at Staten Island, Gallinger Hospital in Washington, D. C., and to three clinics in Virginia (Richmond, Arlington, and Alexandria) for making their cases available for analysis.

Tables 2, 3, and 4 (seronegative primary, seropositive primary, and secondary syphilis) show the results of schedules employing procaine penicillin with aluminum monostearate and schedules employing crystalline penicillin G in aqueous solution through 15 months of posttreatment observation. Procaine penicillin was administered in one, two, or four injections, with total dosages ranging from 300,000 units to 4,800,000 units. The aqueous penicillin schedules employed total dosages of 2,400,000 units or 4,800,-000 units, administered over an 8-day period with 2-hour intervals between injections.

Chart 2 is based on the figures for secondary syphilis presented in table 4. The first section of the chart is a comparison of cumulative re-treatment rates and rates of seronegativity for procaine penicillin schedules of 300,000 units, 1,200,000 units, and 2,400,000 units administered in one injection. From the limited data available, it would appear that 2,400,000 units are more effective than the small dosage schedules in the treatment of secondary syphilis.

The 2,400,000-unit, one-injection schedule is compared in the second section of

chart 2 with an equal amount of procaine penicillin administered in two 1,200,000-unit injections 4 or 7 days apart and with 2,400,000 units of crystalline penicillin G in aqueous solution, administered every 2 hours over an 8-day period. Both procaine schedules (one or two injections) compare favorably with the aqueous penicillin schedule during the 15 months of posttreatment observation shown.

The third section of chart 2 presents the results of two schedules employing 4,800,000 units. The procaine schedule consisted of four injections of 1,200,000 units administered at weekly intervals; the aqueous schedule covered an 8-day period, with injections at 2-hour intervals. Cumulative re-treatment rates for these two schedules are approximately the same throughout the observation period.

These preliminary figures suggest that procaine penicillin administered in one, two, or four injections may be effective in the treatment of early syphilis. A greater volume of cases and a longer observation period will be necessary to verify this impression.

Reference

1. ISKRANT, A. P.; BOWMAN, R. W.; DONOHUE, J. F.: Techniques in evaluation of rapid antisyphilitic therapy. Pub. Health Rep., 63: 965-977, July 23, 1948.

Evaluating Epidemiologic Policy: Illustrated by an Analysis of Current Epidemiologic Policy on Field Investigation of Positive Blood Reports¹

Frederick Plotke, M. D.,² Amelia H. Baker,³ Rose G. Fishtein,⁴ M. E. Laughlin,⁵ and Georgene Schreiner ⁶

The quest for greatest efficiency in any venereal disease control program requires constant re-evaluation of procedures and policies. This is a report of a recent evaluation made by the Chicago Venereal Disease Control Program on the current epidemiologic policy regarding the investigation of persons having positive blood tests, as reported by the laboratory on blood specimens sent in by physicians or clinics not affiliated with the Chicago Health Department. On none of thesc cases had the health department received a morbidity report giving a diagnosis of syphilis. The results of two other studies are also used to prove the findings of this evaluation.

Because of insufficient staff to investigate all reported potentially infectious cases of syphilis, it was necessary to reduce the volume of field assignments on positive blood reports.

It seemed probable that early syphilis was much more likely to be found in the younger age group; therefore, 25 years of age was arbitrarily chosen as the factor determining the type of epidemiologic activity to be performed. All persons 25 years of age and under, reported to the Chicago Health Department as having positive blood tests, were eligible for field investigation. All those over 25 years of age were sent a letter only; if there was no response to the letter, no further investigation was made.

When dispositions were made on those cases located through field investigation, it became obvious that the ratio of early syphilis to syphilis in the later stages was too high to make a 25-year age limit desirable. With a limited staff of epidemiologists, it was also a matter of concern as to whether the present method of investigation of positive blood reports was the most effective method possible.

For these reasons, a study was initiated in April 1948 to determine: (1) the amount of early syphilis found in positive blood reports eligible for field investigation, i. e., in persons 25 years of age and under; and (2) the most effective method of investigation—a letter, followed by field investigation when necessary, or an initial field visit.

The cases covered in the study were those positive bloods reported from April 1 through June 30, 1948, by physicians and clinics not affiliated with the Chicago Health Department.

A report of the study follows:

- 1. Grouping: Letters were sent to 141 persons, with subsequent field investigation on those who did not respond; 139 persons were assigned for an initial field visit.
- 2. Comparability: The two groups were comparable as to age, race, and sex. The median age was 23 years.
 - 3. Results:
- (a) Early syphilis found: Of the total group of 280 suspects, 155 were found and examined; of these 155, 140 (90 percent) were found to be infected with syphilis. Only 14 were found to be not infected. One case was closed as noncooperative. Therefore, 50 percent of the total of 280 persons in the study were infected with syphilis. Since 80 percent of those infected were diagnosed as having primary, secondary, or early latent syphilis, it ap-

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² Vencreal Disease Control Officer.

³ Director, Epidemiology Section.

⁴ Supervisor, Field Unit, Epidemiology Section.

⁵ Director, Statistics Section.

⁶ Statistician.

peared probable that the 25-year age limit for field investigation was much too low.

(b) Epidemiologic activity: Of the 141 cases to whom letters were sent, 32 percent reported and were closed satisfactorily with no field work necessary. Fifty percent of the 72 suspects whose letters were not returned and who did not report were brought in through field investigation. Only 17 percent of the 24 suspects whose letters were returned unclaimed were examined as a result of field work, indicating that with a limited staff, field work on this group is not sufficiently profitable to justify itself. (This is illustrated by table 1.) Therefore, 62 percent of the 141 cases who were sent a letter, followed by field work, were examined and closed satisfactorily. In the group assigned originally to the field, 49 percent reported. The difference between these two percentages is statistically significant.7

Table 1.—Disposition of 141 cases to whom letters were originally sent

Letters sent	141
Examined as a result of letter	45
(32 percent of 141)	-
Letters not returned	72
Examined as a result of visit	38
(50 percent of 72; 27 percent of 141)	
Letters returned	24
Examined as a result of visit	4
(17 percent of 24; 3 percent of 141)	

It would seem then that the best policy for tracing cases with positive blood reports is the initial letter, with field investigation done on those cases wherein the letter is not returned unclaimed.

Table 2 shows the disposition of the total number of cases, and table 3 shows the diagnoses of those found to be infected.

It seemed advisable for us, therefore, to adjust our age limit upward if a divid-

Table 2.—Disposition of cases, by method of tracing

	m 1	Metho traci	
Disposition	Total cases	Field investi- gation	Let- ter
Total cases	280	139	141
Examined, not infected Placed under treatment	14 114	6 49	8 65
Already under treatment Unable to locate Out of jurisdiction	26 92 19	13 53 11	13 39 8
No further investigation desired	1		1
Other	14	7	7

ing line could be established which would encompass the majority of infectious suspects, while not exceeding the number of cases which could be handled by the existing staff.

In order to substantiate the supposition that a 25-year age limit was too low, two previous studies were analyzed in relation to diagnosis and age.

From a study, "Penicillin in the Abortive Treatment of Syphilis," (1) made on 1,069 named sexual contacts to primary and secondary syphilis received by the Chicago Health Department within the period August 25, 1947, to August 24, 1948, it was learned that the median ages for this group were as follows:

	Years
Total group	26. 2
	1
White male	34, 4
White female	27.8
Negro male	26. 9
Negro female	24.3

Since all these contacts were potential early syphilis cases and the median age was as high as 34.4 years in the white male group and 26.2 years for the entire group, it is obvious that positive blood reports should be investigated to encompass a higher age group—35 years of age, at least.

An analysis was also made of early syphilis morbidities for a 6-month period, July to December 1948. The median ages of these primary and secondary

⁷ Significance: If two means or two proportions differ by more than twice the value of the standard error of the difference, the difference is said to be "significant," i. e., more than is easily likely to have arisen by chance. In fact, such a difference would arise by chance, roughly, once in 20 times.

Table 3.—Diagnosis of infected cases, by disposition

			Disposition					
Diagnosis	Total infe	cted cases	Placed treat		Already under treatment			
	Number	Percent	Numher	Percent	Numher	Percent		
Total cases	140	100.0	114	100, 0	26	100.0		
Primary syphilis	4 19 90 12 5 7 1 2	2.8 13.6 64.3 8.6 3.6 5.0 .7 1.4	4 11 75 12 2 7 1	3.5 9.6 65.8 10.5 1.8 6.1 .9 1.8	8 15	30.8 57.7		

syphilis patients corresponded with the ages of the abortive treatment study. Further analysis of the figures in this study showed the following interesting factors:

- 1. Eighty percent of syphilis found in persons 25 years of age and under was primary, secondary, or early latent.
- 2. Seventy-two percent of syphilis found in persons 35 years of age and under was primary, secondary, or early latent.
- 3. Fifty-six percent of all syphilis reported was diagnosed as primary, secondary, or early latent.
- 4. Of total early syphilis reported, 44 percent was in persons 25 years of age and under, whereas 81 percent was in persons 35 years of age and younger.

Therefore, if the positive blood reports follow the same pattern as morbidity reports (which has been the case so far), it would appear that by raising the age limit to 35 years, a better proportion would result between the number of early syphilis cases and the total number of infected cases placed under treatment. At the same time, the amount of early syphilis found would increase.

Summary

In a study conducted by the Chicago Venereal Disease Control Program during a 3-month period (April 1 to June 30, 1948) to determine the most effective epidemiologic policy in the investigation of 280 positive blood reports, results show that:

- 1. A letter, followed by field investigation on those persons failing to respond, was successful in 62 percent of the assignments. An initial field visit with no letter was successful in only 49 percent of the cases.
- 2. Of those who were sent a letter, 32 percent reported without field investigation; the letter technic therefore reduces considerably the volume of field work required.
- 3. An additional 27 percent of the letter group, whose initial letter had apparently been delivered but who did not report, were brought in through field investigation.
- 4. In cases wherein the letter was returned unclaimed, field investigation was shown to be unprofitable.
- 5. Fifty percent of the total group of 280 persons were found to be infected, 80 percent of these being diagnosed as having early syphilis. This indicates that the 25-year age limit determining a field assignment was much too low.

In an analysis of figures obtained from a study of 1,069 named sexual contacts to primary and secondary syphilis for a 1-year period, August 1947 to August 1948, the median age of this group was found to be 26.2 years. The median age, broken down by race and sex, was as high as 34.4 years for the white males.

A study of syphilis morbidities for the period July to December 1948 indicated that by raising the age limit for field investigation to 35 years, a better proportion between the number of early syphilis cases and the total number of infected cases placed under treatment could be established.

Conclusions

From this analysis, the best policy toward investigation of positive blood reports (without a syphilis morbidity report) by a limited staff of field workers appears to be as follows:

- 1. All suspects whose names are received on positive blood reports should be sent a letter requesting them to report to the health department or to their private physician.
- 2. Those persons 35 years of age and under, to whom this letter is delivered but who do not respond, should be assigned to the field for investigation.

Reference

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The Control of Syphilis in Iowa

Ralph H. Heeren, M. D., Ph. D., M. P. H., Albert P. Iskrant, Principal Statistician, and Richard S. Hibbets, Health Program Representative.

In recent years there has been much discussion of the venereal disease control program in terms of its success in controlling syphilis. In the October 1948 Statistical Letter of the Division of Venereal Disease, United States Public Health Service, the question was asked, "How is your State doing?" and certain factors were mentioned which would allow evaluation of syphilis control in a given area.

In Iowa, we visualize a program designed to reduce to a minimum death and disability due to syphilis through the following means: (1) reduction in the number of persons acquiring syphilis; (2) finding and treating early syphilis to cure the disease and to prevent spread of infection; and (3) finding and treating all syphilis to prevent late disabling syphilis or death.

In this paper we shall consider the rates of mortality, infant mortality, and admissions to mental institutions as indicative of death and disability due to syphilis.

Mortality

While we do not know the true mortality rate from syphilis, we believe that for trend purposes the recorded mortality rate is reliable. Between 1936 and the present time we know of no factors which would decrease either the ability of Iowa physicians to diagnose syphilis as a cause of death or their willingness to report it if diagnosed. In 1936, the year in which the Nation-wide venereal disease control program was initiated, the mortality rate from syphilis in Iowa was 10.5 per 100,-000; in 1947 it was 6.5 (table 1). It can be seen from chart 1 that this reduction parallels that of the Nation as a whole and that of United States Public Health Service Region VII, which corresponds roughly to the West North Central States.

¹ Acting Director, Division of Venereal Disease Control, Iowa State Department of Health.

² U. S. Public Health Service.

Table 1.—Mortality from syphilis in Iowa, Region VII, and the United States, 1933–47 ¹

[Rate per 100,000 population]

	Mortality—									
Year	Due to syphilis				Due to par	resis	Due to syphilis (except paresis)			
	Iowa	Region VII	Continen- tal United States	Iowa	Region VII	Continen- tal United States	Iowa	Region VII	Continen- tal United States	
1933 1934 1935 1936 1937 1938 1939 1940 1941 1942 1943 1944 1945 1946 1947	10. 5 11. 7 8. 8 10. 5 9. 8 8. 0 7. 0 8. 8 8. 0 7. 7 8. 4 7. 3 6. 1 6. 5	11. 7 12. 7 12. 6 14. 3 12. 6 12. 5 11. 5 11. 6 11. 2 10. 2 10. 3 9. 7 8. 5 7. 9	15. 1 15. 9 15. 4 16. 2 16. 1 15. 9 15. 0 14. 4 13. 3 12. 2 12. 1 11. 3 10. 7 9. 3 8. 8	3. 2 3. 1 2. 3 3. 3 2. 4 1. 8 2. 3 1. 9 2. 8 2. 5 2. 1 2. 1 2. 2 2. 3	3. 1 3. 4 3. 6 3. 5 2. 9 2. 8 2. 3 2. 9 2. 8 2. 5 2. 7 2. 6	3.6 3.8 3.6 3.5 3.2 3.4 3.4 3.5 3.3 3.9	7. 3 8. 6 6. 5 7. 2 7. 4 6. 2 5. 7 5. 1 6. 0 5. 5 5. 6 5. 6 5. 1 3. 8	8. 6 9. 3 9. 6 10. 8 9. 7 9. 6 8. 7 9. 3 8. 3 7. 4 7. 8 7. 0 5. 9	11. 5 12. 1 11. 8 12. 7 12. 9 12. 4 11. 6 11. 0 10. 1 8. 8 8. 6 7. 8 7. 4 6. 4	

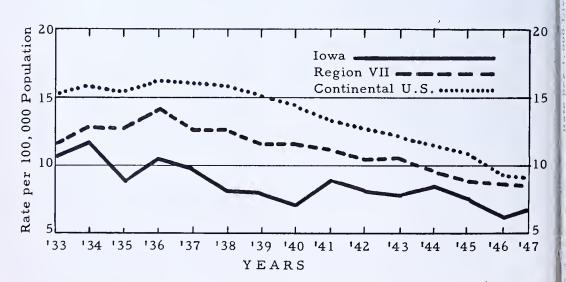
¹ National Office of Vital Statistics, U. S. Public Health Service. (Regional data computed as weighted aver ages by the Division of Venereal Disease.)

Chart 1

MORTALITY from SYPHILIS

in Iowa, Region VII, and the United States

1933 - 1947



Infant Mortality.—In the 4-year period 1944–47, we have had reported in Iowa only 3 deaths from syphilis in children under 1 year of age (table 2). The rate has been reduced from 0.40 per 1,000 live

births in 1936 to 0.02 in 1947. Our record in this phase of syphilis control compares favorably with that of the United States as a whole and with that of Region VII (chart 2).

Table 2.—Infant mortality from syphilis in Iowa, Region VII, and the United States, 1933–47 ¹

[Rate per 1,000 live births]

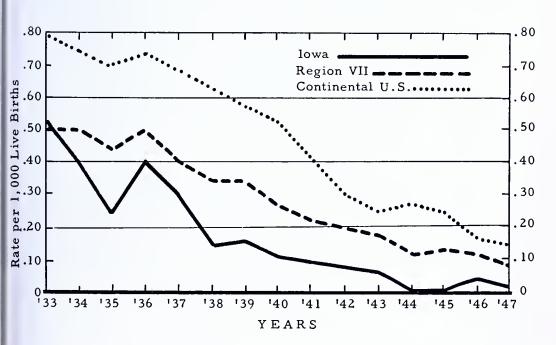
Year	Iowa	Region VII	Continental United States	Year	Iowa	Region VII	Continental United States
1933	0. 53 . 40 . 24 . 40 . 29 . 14 . 16 . 11	0.50 .50 .44 .50 .40 .34 .34	0. 79 . 74 . 70 . 73 . 69 . 63 . 57 . 53	1941 1942 1943 1944 1945 1946 1947	0.09 .08 .06 .00 .00 .04 .02	0. 21 . 19 . 17 . 11 . 13 . 11 . 07	0. 41 . 30 . 25 . 27 . 25 . 16 . 14

¹ National Office of Vital Statistics, U. S. Public Health Service. (Regional rates computed as weighted averages by the Division of Venereal Disease.)

Chart 2

INFANT MORTALITY from SYPHILIS in Iowa, Region VII, and the United States

1933 - 1947



Admissions to Mental Institutions

In 1946 the rate of admissions per 100,000 population to Iowa State hospitals for psychoses due to syphilis was 2.5. This represented 6.8 percent of all first admissions with a psychosis to State hospitals (table 3). From 1936 to 1946, the rate per 100,000 population decreased by 39 percent (chart 3).

Thus, syphilis mortality in Iowa has decreased 38 percent since 1936, infant mortality has decreased 95 percent, and admissions to State hospitals with psychoses due to syphilis have decreased 39 percent. We believe that we have been eminently successful in reducing mortality and disability due to syphilis. But have we also reduced the reservoir of syphilis?

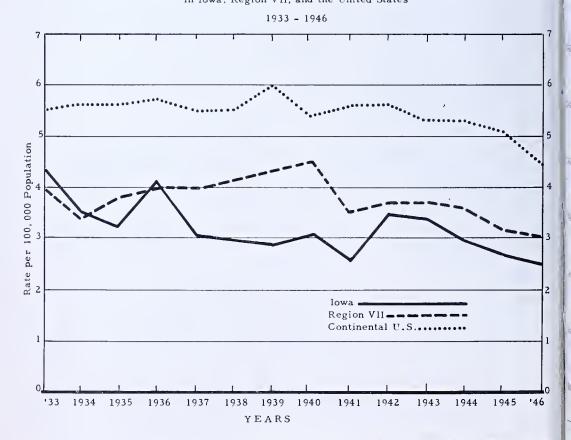
Table 3.—First admissions to State hospitals with psychoses due to syphili in Iowa, Region VII, and the United States, 1933–46 ¹

	Rate per 100,000 population									Rate per 100 first admissions			
Year	Total psychoses due to syphilis Paresis		Other syphilis of the central nervous system			Total psychoses due to syphilis							
	Iowa	Region VII	Continental United States	Iowa	Region VII	Continental United States	Iowa	Region VII	Continental United States	Iowa	Region VII	Continental United States	
1933	4. 4 3. 5 3. 2 4. 1 3. 1 2. 9 3. 1 2. 6 3. 5 3. 4 3. 0 2. 7 2. 5	4. 0 3. 4 3. 8 4. 0 4. 0 4. 1 4. 3 4. 5 3. 5 3. 7 3. 6 3. 2 3. 0	5. 5 5. 6 5. 6 5. 7 5. 5 6. 0 5. 4 5. 6 5. 3 5. 3 5. 1 4. 4	3.8 3.2 2.8 3.8 2.7 2.6 2.7 2.4 2.1 3.2 2.6 2.6 2.6 2.1 2.2	3. 4 3. 1 3. 3 3. 4 3. 4 3. 5 3. 8 2. 8 3. 0 3. 2 2. 8 2. 7	4. 7 4. 6 4. 7 4. 8 4. 7 5. 1 4. 7 4. 8 4. 7 4. 6 4. 5 3. 9	0. 5 .3 .4 .3 .4 .4 .3 .6 .6 .6 .3 .8 .4 .7	0.6 .3 .5 .6 .7 .7 .7 .7 .7 .7 .4 .4	0.9 .9 .9 .9 .8 .8 .8 1.0 .7 .6 .6	9. 4 7. 6 8. 7 6. 6 7. 5 8. 2 7. 0 7. 8 7. 7 6. 7 6. 8	10. 0 8. 9 9. 6 9. 4 9. 3 9. 8 10. 0 8. 4 9. 2 9. 1 8. 6 7. 7 8. 1	11. 0 11. 2 10. 9 10. 6 10. 3 11. 0 10. 1 9. 8 9. 6 9. 2 8. 8 8. 6 7. 8	

¹ Bureau of the Census: Patients in Hospitals for Mental Disease, 1933–37, and Patients in Mental Institutions, 1938–46; Current Population Reports.

Chart 3

FIRST ADMISSIONS to STATE HOSPITALS with PSYCHOSES due to SYPHILIS in Iowa, Region VII, and the United States



To evaluate this phase of the program, we shall use morbidity data and the prevalence of syphilis in selected groups.

Morbidity Reporting of Syphilis

It is realized that morbidity reporting of syphilis is not synonymous with incidence of the disease. For instance, of all cases reported in a given period, some are in the early and some are in the late stages of syphilis; nor can the trend of cases reported in the primary and secondary stages be interpreted as the trend in incidence because of possible changes in completeness of reporting, effectiveness of case-finding methods, and other factors. Morbidity reporting by private physicians inIowa depends, large extent, on measures taken from time to time by the health department to improve it. While we do not believe that the trend of such reporting indicates the trend in cases coming to medical attention, we believe that the trend in cases reported by clinics and institutions reflects the true admission rate to these treatment sources. Table 4 and chart 4

Table 4.—Cases of primary, secondary, and early latent syphilis reported by clinics and institutions in Iowa, Region VII, and the United States, third quarter 1941 to second quarter 1949

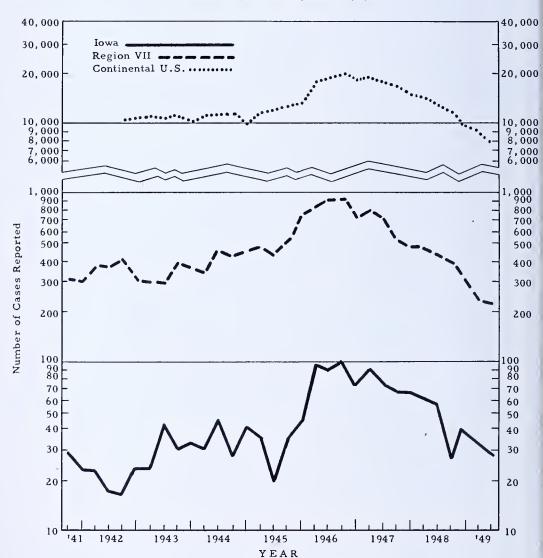
	Primar	y and second	ary syphilis	Early latent syphilis			
Period	Iowa	Region VII	Continental United States	Iowa	Region VII	Continental United States	
1941: Third quarter Fourth quarter	29 23	301 297		47 45	753 670		
1942: First quarter Second quarter Third quarter Fourth quarter	22 17 16 23	373 363 397 303	10, 286 10, 436	62 96 82 122	821 799 658 522	25, 656 27, 352	
1943: First quarter Second quarter Third quarter Fourth quarter	23 43 30 33	290 289 385 355	10, 981 10, 958 11, 057 10, 260	103 59 33 40	467 523 726 786	29, 787 28, 163 24, 475 20, 392	
1944: First quarter Second quarter Third quarter Fourth quarter	26	342 449 423 445	11, 097 11, 203 11, 266 9, 794	44 26 22 68	742 649 584 677	21, 755 20, 387 16, 890 15, 298	
1945: First quarter Second quarter Third quarter Fourth quarter	19	483 431 516 732	11, 601 12, 107 12, 526 13, 635	58 22 27 39	703 718 555 967	17, 232 20, 764 19, 318 17, 780	
1946: First quarterSecond quarterThird quarterFourth quarter	95 89 100 71	834 923 937 715	17, 808 18, 640 19, 654 18, 537	49 44 66 34	1, 041 1, 009 898 718	20, 754 19, 788 18, 835 18, 160	
1947: First quarter Second quarter Third quarter Fourth quarter	71 66	795 704 514 470	18, 555 17, 242 16, 372 14, 750	37 29 44 43	677 586 689 529	19, 085 19, 402 18, 975 16, 569	
1948: First quarter Second quarter Third quarter Fourth quarter	54 26	464 424 381 295	14, 008 12, 901 11, 481 9, 671	43 42 38 40	565 495 445 425	16, 381 17, 802 15, 956 13, 631	
1949: First quarterSecond quarter 1	31 26	228 220	8, 868 7, 516	42 29	447 401	15, 334 14, 439	

¹ Provisional data.

TREND of MORBIDITY REPORTING of PRIMARY and SECONDARY SYPHILIS by CLINICS and INSTITUTIONS

in Iowa, Region VII, and the United States

3rd Quarter 1941 - 2nd Quarter 1949



show the cases of primary, secondary, and early latent syphilis reported, by quarters, for clinics in Iowa. It will be noted that Iowa shows the same trend as Region VII and the United States.

In an editorial entitled "Is the Incidence of Syphilis Decreasing?" in the July 1949 issue of The Journal of Venereal Disease Information, it was pointed out that the decrease in primary and secondary cases reported could be

interpreted as a decrease in cases occurring under certain circumstances. We believe that the decline in early syphilis cases reported by clinics and institutions in Iowa indicates a decrease in the incidence of syphilis because (1) the early latent cases reported have decreased; (2) there has been no diminution in case-finding activities for early syphilis; and (3) to our knowledge there has been no increase in cases being treated by

private physicians in Iowa. We may conclude, therefore, that the incidence of syphilis is decreasing in areas served by clinics in Iowa as well as in the continental United States.

Prevalence of Syphilis

We do not know the prevalence of syphilis in Iowa. Usually the rate of positive results of the serologic test for syphilis is taken as an estimate of the prevalence of syphilis in a group. On this basis, it was estimated that the prevalence of syphilis in Iowa among selectees through August 1941 was 15.9 per 1,000 (1).

If we could now test a similar group of men, using the same criteria for the estimate of prevalence, we could determine increases or decreases since 1941. In lieu of other data, we believe that

the trend of positivity in persons marrying and in women having babies may give us some clues to the trend of syphilis prevalence in Iowa. Table 5 gives the results of the blood tests for prenatal and premarital examinations performed in the Iowa State Hygienic Laboratory between July 1941 and December 1948, the positive and doubtful tests on an individual being counted throughout this period. We do not feel that the positive and doubtful results should be added to estimate prevalence, as the variation in the doubtful rate from period to period is very erratic and suggests association with factors other than syphilis prev-We believe that the trend in positives is probably indicative of the trend in syphilis prevalence.

We are cognizant of the fact that the proportion of persons with positive results who have been adequately treated

Table 5.—Results of prenatal and premarital serologic testing for syphilis in Iowa, July 1941–December 1948 ¹

[Rate of positive and doubtful per 1,000 persons tested]

		Prenatal		Premarital			
Period	Number tested	Positive ² rate	Doubtful ² rate	Number tested	Positive ² rate	Doubtful ² rate	
1941: July 1-Dec. 30	19,693	7.6	5.8	13, 618	4. 6	4. 4	
1942: Jan, 1-June 30	21, 939 20, 171	5. 8 5. 3	5. 4 3. 9	11, 695 10, 938	5. 6 6. 6	6.2 2.7	
1943: Jan. 1~June 30 July 1–Dec. 30	20, 987 18, 467	7. 4 7. 6	4.9 4.7	11, 792 13, 368	7. 6 9. 7	1.6 2.7	
1944: Jan. 1-June 30	19, 716 18, 269	6. 7 5. 6	5. 4 4. 2	15, 296 15, 358	8. 8 8. 0	3.0 1.6	
1945: Jan. 1-June 30 July 1-Dec. 30	17, 790 18, 041	3. 2 4. 5	5. 2 5. 5	15, 419 21, 519	8. 0 8. 3	2. 5 5. 2	
1946: Jan. 1-June 30 July 1-Dec. 30	28, 251 29, 007	4.6 6.0	6. 5 7. 5	28, 877 27, 013	8. 6 9. 3	6. 9 7. 3	
1947: Jan. 1-June 30 July 1-Dec. 30	27, 735 25, 426	5. 9 5. 8	8.3 6.3	25, 165 25, 427	8. 0 8. 9	7. 6 5. 5	
1948; Jan. 1-June 30 July 1-Dec. 30	27, 438 25, 836	5. 7 4. 9	7.4 7.1	23, 604 23, 720	8. 7 8. 3	4.3 3.8	

All tests performed by the Iowa State Hygienic Laboratory.

² All positive and doubtful rates are unduplicated; only the initial result is counted for each individual.

is probably higher in 1948 than in 1941, but in the absence of information as to which people examined had "syphilis needing treatment," we believe that the proportion with positive tests is our best estimate of trend.

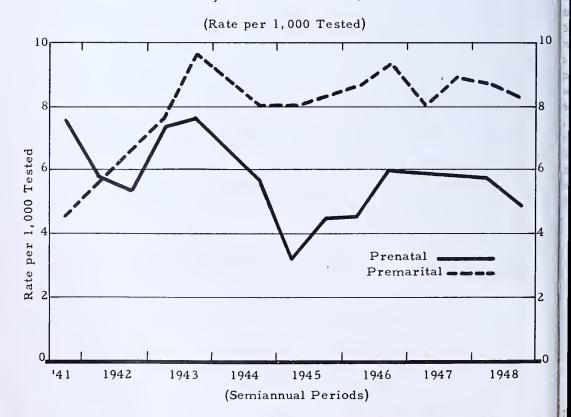
The trend of positive results of prenatal and premarital serologic testing (per 1,000 persons examined) from July 1941 to December 1948 has been plotted in chart 5. It will be noted that there has been no obvious decrease in the percent positive of persons marrying, although possibly there may have been a reduction in the percent positive among women having babies. Since these are the results of tests for all pregnancies, not the first only, and since many women have more than one baby, we may expect the percent positive to be lower than the per-

centage on the first pregnancy, if previous tests resulted in the diagnosis and treatment of syphilis. The fact that we do not know the results of these tests by the number of the present pregnancy and the fact that most women having babies have been tested as part of their premarital examination probably account for the lower rate of prenatal than premarital positive These data are not available by color, sex, and age, but it is assumed that premarital testing is approximately evenly divided between males and females.

From data published by the Division of Vital Statistics (2), indicating the number of marriages and births in Iowa from 1941 to 1948, it appears that practically all bloods for premarital and prenatal examinations are tested at the State Hy-

Chart 5

TREND of POSITIVE RESULTS of PRENATAL and PREMARITAL SEROLOGIC TESTING for SYPHILIS in IOWA July 1941 - December 1948



gienic Laboratory. The percentage of Negro births was remarkably constant during that period, varying from a low of 0.58 percent to a high of 0.66 percent; the percentage of Negroes marrying also varied little and showed no tendency to increase. We can therefore assume that the rates of positivity are probably not affected by changes in the racial composition of the groups tested.

Although the results of these tests are not available by age, we can obtain the age of bride and groom from the reports of the Division of Vital Statistics (2). A study of the ages over the period 1941 to 1948 indicates no great change in the composition of the groups marrying. Moreover, in an area where data are available by age, an analysis made by the Division of Venereal Disease, United States Public Health Service, indicated little difference in trend between the crude and age-adjusted rates. On the basis of these data, we believe that there has been no decline in the prevalence of syphilis in Iowa as indicated by a positive blood. may appear strange that the estimated prevalence of syphilis should remain constant, with mortality decreasing constantly and new syphilis decreasing for the past $2\frac{1}{2}$ years. However, it must be remembered that, prior to the decrease, new cases were increasing for the four previous years and that presumably the reduction in incidence has not yet affected the prevalence of syphilis as indicated by a positive blood. This means that our potential treatment load remains high and that we must continue our efforts to find and treat syphilis in order to maintain our reduction in mortality and in psychoses due to syphilis.

Summary

We have attempted to evaluate the syphilis control program in Iowa in terms of its accomplishment since 1936. We find that:

- 1. Between 1936 and 1947, the mortality rate from syphilis was reduced 38 percent (from 10.5 to 6.5 per 100,000).
- 2. For the same period, the infant mortality rate has been reduced 95 percent (from 0.40 to 0.02 per 1,000 live births).
- 3. From 1936 to 1946, the rate of admissions to mental institutions with psychoses due to syphilis decreased by 39 percent (from 4.1 to 2.5 per 100,000 population).
- 4. On the basis of morbidity reports from clinics and institutions, we conclude that the incidence of acquired syphilis in Iowa has been decreasing over the past 2 years.
- 5. Based on the results of serologic testing of persons marrying and women having babies, there has been no obvious decline in the prevalence of syphilis over the past 7 years. Thus the reservoir of syphilis remains with us, and we must continue our case-finding and treatment program at an undiminished pace in order to retain the gains we have made.

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CURRENT LITERATURE

Note.—Abstracts of all articles listed below are available on request. In addition, abstracts of articles concerned with venereal diseases or related subjects which have been published in the better-known journals during the past 25 years are in the files. These are open to workers in the field. An asterisk (*) before a title indicates that the article is abstracted below.

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*Treatment of neurosyphilis with penicillin combined with artificial fever. Norman N. Epstein and Jules M. Key. 60: 543– 557, Oct. 1949.

Treatment of neurosyphilis with penicillin combined with artificial fever. Norman N. Epstein and Jules M. Key. Arch. Dermat. & Syph., 60: 543–557, Oct. 1949.

A total of 87 patients with various forms of neurosyphilis was treated with penicillin combined with artificial fever therapy. The work began in March 1945. Penicillin was administered in two forms: aqueous penicillin sodium, intramuscularly, every 3 hours over a 14-day period, for a total dose of 4,500,000 units, and penicillin calcium suspended in peanut oil containing 4.5 percent white wax, administered in daily single intramuscular injections of 300,000 units each for 20 days, for a total of 6,000,000 units. Artificial fever therapy was administered by the blanket method during and subsequent to the penicillin course. Five hours of a temperature over 40° C. was considered a

single treatment. Most of the patients received a total of 50 hours of fever therapy.

Of this group, 55 patients have been followed for 120 days or longer, some as long as 2 years or more. Definite improvement in the spinal fluid signs was noted in 70 percent of the patients during the first year of posttreatment observation and in 87 percent of those observed for a longer period. Serologic tests became negative in only 14.5 percent of the patients during the first year of observation and did not change during the second year.

Severe Herxheimer reactions in the central nervous system were noted in two patients. Fever therapy was well tolerated by all but two patients.

The combination of penicillin and fever therapy gave better effects than did chemotherapy combined with fever therapy. The effects of artificial fever combined with penicillin therapy should continue to be investigated because of the known effects of artificial fever on the clinical course and spinal fluid abnormalities of neurosyphilis and the experimental data which indicate that elevation of temperature in vitro and in vivo enhances the spirocheticidal properties of penicillin.

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STATISTICS

linic and Epidemiologic Data Reported to the Public Health Service by State and Territorial Health Departments, Fiscal Years 1947–49

Clinic and epidemiologic data	1947	1948	1949
iagnostic examinations in public clinics	1, 764, 045	2, 328, 002	2, 276, 975
ercent of examinations in which one or more V. D. was found	29.8	21.0	20.3
revious untreated sypbilis cases found per 100 examined revious untreated primary and secondary syphilis cases found per 100	9.3	6.7	5. 7
examined.	3.2	1.9	1.3
recent of early symbilis discovered sent to R. T. C. for treatment.	61.0	65. 5	57. 0
umber of contact investigations completed	476, 368	408, 054	380, 079
umber of other suspect investigations completed	177, 169	164, 003	153, 435
pproximate number of contacts obtained per primary and secondary	1 70	0.00	0.70
syphilis patient	1. 79	2.30	2.53
gation per primary and secondary patient.	. 54	.70	. 72
pproximate number of syphilis infections brought to treatment through			
contact investigation per primary and secondary patient	. 30	.37	. 40
pproximate number of primary and secondary syphilis brought to treat-			
ment through contact investigation per primary and secondary patient.	. 15	. 17	. 18
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 ${\bf Source: Quarterly\ Venereal\ Discase\ Control\ Activity\ Report\ (PHS-Form\ 8954-A)\ and\ Special\ Semi-annual\ abulations\ of\ Contact\ Investigation\ Data.}$

FSA-PHS-Division of Venereal Disease, Office of Statistics, 1/18/50 (API-JWR) kc.





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Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced. with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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Editor: THEODORE J. BAUER, Medical Director Chief, Division of Venercal Disease

The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Pocuments, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription Price: Domestic 75 cents a year; foreign \$1.15

Editorial

Mortality From Syphilis

One of the objectives of the syphilis control program is to reduce the amount of disability and death due to syphilis. It may be seen from the tables at the end of this publication that the death rate has decreased from 16 per 100,000 population in 1938 to 8 in 1948. That this improvement may be attributed to control measures is shown by the fact that, while mortality from paresis started to decline in 1923 as soon as malaria therapy was introduced in the United States, deaths from other types of syphilis did not decline until after 1936, when the Nation-wide venereal disease control program was initiated. The rates have been downward ever since.

Although the death rate from paresis in the nonwhite population seemed resistant for a while to control measures, particularly in the years 1942 to 1946, later years have shown improvement, and the considerable decline

is now consistent for color and sex in all types of late syphilis.

Likewise, the infant mortality rate from syphilis has declined since the initiation of the National Venereal Disease Control Program. Up to 1937 the infant mortality rate from syphilis declined at about the same rate as the infant mortality rate from all causes, but since 1938 the decline in infant mortality due to syphilis has been much steeper.

These mortality data are extremely encouraging and give considerable hope that mortality from syphilis will eventually be reduced to negligible proportions. Nevertheless, it is well to bear in mind that it has not yet reached that desired level. In 1948, 12,000 deaths from syphilis were recorded (not including stillbirths and abortions), of which 438 were infants under one year of age.

Theodore J. Bauer, Medical Director Chief, Division of Venereal Disease

Procaine Penicillin G in the Treatment of Gonorrhea

Ralph B. Hogan, Senior Surgeon,¹ Edgar B. Johnwick, Senior Surgeon,² Leland J. Hanchett, Senior Surgeon,³ Fred W. Harb, Senior Surgeon,⁴ United States Public Health Service, and Ottis L. Adar, M. D.⁵

Since the introduction of penicillin in oil and beeswax (POB) in the treatment of venereal diseases, the usually accepted dosage for gonorrhea has been 300,000 units. Based on reports in the literature and on the statement (1) by the Syphilis Study Section of the National Institutes of Health, issued December 1, 1947, the Division of Venereal Disease of the United States Public Health Service (2) early in 1948 recommended 300,000 units of POB as an acceptable schedule.

With the 300,000-unit dosage, occasional clinical and bacteriologic failures have occurred. Some of these failures have been obvious reinfections; in other cases, the clinical symptoms have shown little tendency to subside, but there has been no reason to believe that reinfection had occurred. Tucker (3) has recently recommended 0.5 mg. (500 units) of procaine penicillin per kilogram of body weight (approximately 0.12 cc., or 36,000 units, for the average adult) as a routine therapeutic dosage in uncomplicated acute gonorrhea. Inasmuch as this represents only one-eighth of the usually accepted dosage (300,000 units of penicillin G), it seemed desirable to confirm these observations. A study was undertaken to verify (1) the effectiveness of small doses of procaine penicillin in the therapy of gonorrhea, (2) the minimal effective dose, and (3) the validity of a 48-hour posttreatment culture as a test of cure when procaine penicillin is used as the therapeutic agent.

Methods

Origin of Cases

The patients studied were drawn from four sources: Eastern Medical Center, Durham, N. C.; Midwestern Medical Center, St. Louis, Mo.; United States Public Health Service Medical Center, Hot Springs National Park, Ark.; and Durham City-County Clinic, Durham, N. C. A total of 135 patients were included in this study: 99 Negro males, 17 Negro females, 13 white males, and 6 white females.

Patients treated at the first three centers were hospitalized to eliminate as far as possible the question of reinfection. The patients at the Durham clinic were treated on an out-patient basis to permit a longer follow-up (patients are reluctant to be hospitalized even 5 days for the treatment of gonorrhea) for the purpose of testing the validity of 5 days' observation as an indication of cure. To reduce the probability of reinfection to a minimum in this latter group, the patients were carefully interviewed for contacts, and all contacts were treated with 300,000 units of procaine penicillin in oil containing 2 percent of aluminum monostearate, regardless of whether or not the presence of the gonococcus was demonstrable.

Therapy

Therapy for 113 patients consisted of a single intramuscular injection of procaine penicillin G in oil containing 2 percent of aluminum monostearate, in dosages of 100, 200, 250, 300, 500, and 1,000 units of penicillin per kilogram of body weight, administered as shown in table 1. To facilitate accurate administration in small quantities, commercial

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Table 1.—Graduated doses of procaine penicillin preparation A used to treat 113 cases of gonorrhea, by units per kilogram of body weight and by total dosage

Units of penicillin per kilogram of	Cubic cent	imeters of pe	nicillin prepa betwe		d for patient	ts weighing
hody weight	80-100 pounds	101-120 pounds	121-140 pounds	141-160 pounds	161-180 pounds	181 pounds and over
100	0.13 .27 .33 .40 .67	0. 17 · 33 · 42 · 50 · 84 1. 67	0. 20 . 40 . 50 . 60 1. 00 2. 00	0. 23 . 47 . 58 . 70 1. 17 2. 33	0. 27 . 53 . 67 . 80 1. 34 2. 67	0. 30 . 60 . 75 . 90 1. 50 3. 00

preparations containing 300,000 units of procaine penicillin per cubic centimeter were diluted 1 to 10 with sterile oil containing 2 percent of aluminum monostearate, which gave a final concentration of 30,000 units of penicillin per cubic centimeter (preparation A).

Twenty-two of the patients at Hot Springs were treated with 1 cc. of another preparation, which consisted of procaine penicillin so diluted in sterile sesame oil as to contain either 12,500, 25,000, or 50,000 units of penicillin per cubic centimeter (preparation B). The dosage in units of penicillin per kilogram of body weight was calculated later. Two of these patients received 300 units of penicillin per kilogram of body weight; two, 650 units; eleven, between 700 and 800; five, 950; and two, 1,000.

Cures and Failures

This study included only cases of acute uncomplicated gonorrhea in which the pretreatment culture was positive and the organism was confirmed as the gonococcus by sugar fermentation. "Cure" was defined as (1) eradication of clinical symptoms and (2) repeated negative cultures for a minimum of 5 days after treatment. Failure was defined as (1) persistence of clinical symptoms or (2) presence of positive cultures 24 hours or longer after therapy.

Results

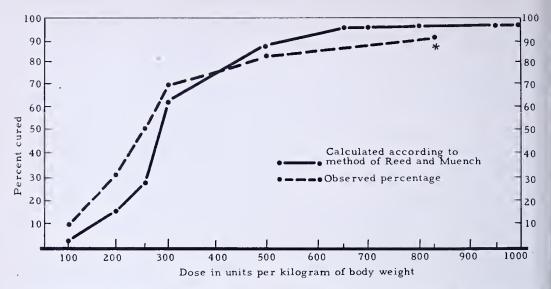
Clinical and Bacteriologic

The clinical and bacteriologic results are presented in table 2 and in figure 1. In this series of 135 cases treated with

Table 2.—Results of treating 135 cases of gonorrhea with graduated doses of procaine penicillin, by units of penicillin per kilogram of body weight and by cure rate

		Observ	ed results		Ca	lculated resu	lts 1
Units of penicillin per kilogram of body weight	Number cured	Number failed	Total cases observed	Percent cured	Expected number of cures	Expected number of failures	Expected percentage of cures
100	1 5 2 23 36 2 11	10 11 2 10 7 0 0 0	11 16 4 33 43 2 11 5	9. 1 31. 2 50. 0 69. 7 83. 8	1 6 8 31 67 69 80 85 93	42 32 21 19 9 2 2 2	2. 32 15. 79 27. 58 62. 00 88. 15 97. 18 97. 56 97. 7
Total	93	42	135		93		91.8

 $^{^1}$ Results calculated according to method of Reed and Muench, in which the dose needed to cure half of the cases equals 281 units of penicillin per kilogram of body weight (CD $_{50}\!=\!281\,u./kg.$).



*Since this rate is calculated on the basis of the entire group receiving between 650 and 1,000 units of penicillin per kilogram of body weight, it is plotted at the midpoint of the dosage—825 units.

FIGURE 1.—Effectiveness of procaine penicillin in the treatment of gonorrhea.

100 to 1,000 units of procaine penicillin per kilogram of body weight, no schedule resulted in complete failure; on the other hand, occasional failures occurred even with the larger doses. Slightly less than 10 percent were cured at 100 units per kilogram of body weight. Increasing the 100-unit dosage 6-fold to 10-fold resulted in a cure rate of 93 percent. As may be seen in figure 1, there is a rapid and pronounced increase in cure rate from approximately 10 to 70 percent with only a 3-fold increase of the 100-unit dosage (100 units to 300 units). A 2-fold to 3.33-fold increase in the 300-unit dosage resulted in a further increase in the over-all effectiveness of 23 percent, bringing the cure rate to 93 percent.

When the cures and failures, by dosage, are calculated according to the Reed-Muench method (4), 100 units of penicillin per kilogram of body weight resulted in 2.3 percent cures and 1,000 units per kilogram in 97.8 percent.⁶

Point of Origin

Table 3 shows the cases by point of origin. When only a few cases were involved, there was a considerable difference in results, despite the fact that preparation A was prepared centrally and distributed to contributing clinics. This, no doubt, reflects the individual variation in susceptibility to penicillin therapy.

Follow-Up at 24 to 144 Hours

Table 4 lists the results of cultures and clinical symptoms of the 42 failures. At 24 hours, cultures were obtained on 27 of these patients, of which 15 (55.6 percent) were positive. Cultures were obtained on 26 of these 42 patients at 48 hours; four (15.3 percent) were positive that had been negative at 24 hours. Cultures were obtained at 72 hours on 10 patients with previous posttreatment cultures; three were positive that had been negative at 24 or at 48 hours or at both (only one was positive that had been negative at both 24 and 48 hours). Cultures taken on 15 additional patients were positive for the first time at 72 to 144 hours; however, in this group, either no previous cultures had been taken or none

⁶ Theoretically, extrapolating according to the method of Bliss, 1,762 units per kilogram of body weight would result in a cure rate of 99 percent and 3,404 units per kilogram of body weight in a cure rate of 99.9 percent (5).

Table 3.—Point of origin of 135 cases of gonorrhea treated with graduated doses of procaine penicillin, by units of penicillin per kilo-gram of body weight and by cure rate

nent		Percent	000000
Out-patient treatment	Durham elinie	Cases treated	8 000080000
Out-patie	Durh	Fail- ures	00000000 m
		Cases	000000000000000000000000000000000000000
	Donogae	enred	32.00 32.00 59.69 80.00 100.00 100.00
	E-	cases	112 833 14, 16 10 10 112
	nter	Fail- ures	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	Hot Springs center	Cases	0 4 4 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
ment	Hot Sp	Cases treated	24 8 8 8 8 8 8 8 2 2 2 111 2 115 1 63
In-patient treatment	er	Fail- ures	47-004-00-1 91
In-pati	St. Louis center	Cases	000440001 6
	St. L	Cases treated	41-04800002 8
	er	Fail- ures	000000000
	am eenter	Cases	1112840008 4
	Durha	Cases treated	17.114.04000 #7
	Units of penicillin per kilogram of body weight		100 200 250 300 300 500 550 530 1,000 1,000 Total

95

Includes 2 eases treated with preparation B. Treated with preparation B.

Table 4.—Results of posttreatment cultures in 42 treatment failures

	Units of penicillin		Numb	er of hours	posttreat	ment		
Failure No.	penicillin per kilo- gram of body weight	24	48	72	96	120	144	Remarks
1	100	SD		PD +	PD +			
2	100	PD +	PD +					
3	100	SD +	+		PD -			
4	, 100	PD -	WD	MPD -				Clinical failure.
5	100	SD +	No D +		PD +			-
6	100	No D	PD +	PD				
7	100	PD +	PD +					
8	100	PD +	PD +					
9	100		PD +					
10	100	SPD +	PD +					
11	200	SMD +	PD +			_		•
12	200	Hazy +		PD +				
13	200	Cloudy +	SPD +		_	_		
14	200	SD +	PD +					1
15	200						PD +	
16	200	Hazy +	PD +	PD +				
17	200						PD	Clinical failure.
18	200	+	+	+	ļ .			
19	200			+	+	+		
20	250	PD		+	+	+		
22	250	PD	PD +		PD +			
23	300	PD -	SD +		<u> </u>	PD +		
24	300	SD -		No D		No D +		
25	300			PD +	PD +	PD +		
26	300			PD +	PD +			
27	300				+	+		

Table 4.—Results of posttreatment cultures in 42 treatment failures—Continued

	Units of penicillin		Numb	er of hours	s posttreatr	nent		
Failure No.	penicillin per kilo- gram of body weight	24	48	72	96	120	144	Remarks
28 .	300			+	+			,
29	300			+	+	+		
30	300			+				
31	300						+	
32	300	_	_			+		
33	300	_		+				
34	590	+	+	PD +				
35	500	SMD -	PD -	PD -				Clinical failure.
.36	500	SPD +	PD +					
37	500		SMD +		SMD -			
38	500	+		D +	•			
39	500		_			PD +		
40	500		- .			PD +		
41	1,000	SD -	PD +					<u>}</u>
42	1,000					+	+	

⁺Positive.

SMD—Slight mucoid discharge.

had been taken since 48 hours. mation is therefore not available as to what percentage of these individuals would have been positive had cultures been taken earlier.

Follow-Up from 6 to 30 Days

Table 5 lists the results of cultures and clinical symptoms of 55 cases followed from 6 to 30 days after treatment. In this group, no case was found to be positive after 5 days that was not positive on the fifth day, with the exception of patients 2 and 10. In the case of patient 2, the culture taken at 6 days was inadvertently the first posttreatment culture obtained. In the case of patient 10, it was the first culture since 48 hours.

The results suggest that cultures taken less than 72 hours after treatment may be unreliable as a test for cure when procaine penicillin is the therapeutic agent.

Similar results have been obtained in previous studies (6, 7) utilizing other The minimum penicillin preparations. period required as a satisfactory test for cure apparently lies between 3 and 6 days.

Discussion

The results of this study indicate that there is a rather wide range in dosage between that which cures an occasional case of gonorrhea and that which cures essentially all cases. A cure rate of ap-

Negative.

WD-Watery discharge. No D-No discharge.

SD-Slight discharge.

SPD-Slight purulent discharge.

PD-Purulent discharge. MPD-Mucopurulent discharge.

Table 5.—Results of posttreatment cultures on 55 patients followed 6 to 30 days

Core No	Units of penicillin per kilo-	-		N	umber o	of days po	sttreatm	ent		
Case No.	gram of body weight	1	2	3	4	5	6	7-10	11-29	30
1	100	VSD -	VSD -			No D		No D		
2	200						PD +			
3	200	PD -	PD -			_	No D			
4	200	•					PD -			
5	200	_		_				_		
6	200	_	_	_	_	_		_		
7	200	_	-		_		_			
8	250	No D		_				_	_	
9	250	VSD -	VSD -			VSD -	VSD -	VSD -		
10	300	Hazy	No D				+			
11	300	_	_		_			_		
12	300		_			-		_		
13	300		_		_		_			
14	300	_			_		_			
15	300	_			_	_	_			
16	300	_	_	_				_		
17	300	_						_		
18	300	_	_		_	_	_			
19	500	_				SD -	SMD -			
20	500	SPD -	_							
21	500	_	_	_				- .		-
22	500					_		_		
23	500	_						_		-0
24	500	_	_			_		_		-
25	500	_				_				_
26	500	_						-		-
27	500		_		-	_		_		_
28	500	SD -						_		_
29	500	_						_		_
30	500		_			_		_		
31	500	_	_	_		_		-		_
32	500							_		_
33	500		_	-	-	-		-		
34	500	_	_)				_		_

Table 5.—Results of posttreatment cultures on 55 patients followed 6 to 30 days—Continued

Case No.	Units of penicillin per kilo-			N	Tumber o	of days p	osttreatm	ent		
Case No.	gram of body weight	1,	2	3	4	5	6	7-10	11-29	30
35	500		_] _		_
36	500	-	_	-	_	-	-			
37	500	-	_					_		
38	500		_	-				_		
39	500	-	_			-	-			
40	500				SD -			_		
41	500	_	_			_	1	-		_
42	500	-	-			_		_		_
43	650		-			-		_		
44	650	WD			_		_	_		
45	750				-		_			
46	760				_		_	_		
47	770			_		_		_		
48	780			-		-		_		
49	950		-			-	_	_		
50	950		-	_	-			_		
51	1, 000		-		-			_		
52	1,000		_	-			-			
53	1, 000		-			-	_	_		
54	1.000					-	-	-		
55	1,000			1		+	+			

⁺Positive.
-Negative.
WD-Watery discharge.

No D—No discharge. SD—Slight discharge. VSD—Very slight discharge. SMD—Slight mucoid discharge. SPD—Slight purulent discharge. PD—Purulent discharge.

proximately 93 percent was obtained with the highest dosage studied (1,000 units per kilogram of body weight). Maximum therapeutic results could therefore be expected from dosages in excess of this amount.

The usual practice among physicians has been to administer a specified number of units of penicillin without regard to body weight. Obviously, if 60,000 units (which represent 1,000 units of penicillin per kilogram of body weight for a patient weighing 60 kg.) were administered to a patient weighing 100 kg., the dosage per kilogram of body weight is

reduced to 600 units. One could expect therapeutic results in such instances to approach more closely those obtained with 500 units (a cure rate of 84 percent) than those obtained with 1,000.

When the dosage is routinely administered without considering body weight, the total dose calculated for a 60-kg. patient should be increased 40 to 50 percent in order to be adequate for individuals with greater body weight.

Summary

The results obtained in the treatment of 135 patients with acute uncomplicated

gonorrhea with procaine penicillin are presented. An occasional cure occurred at 100 units of penicillin per kilogram of body weight; an occasional failure occurred at 1,000 units of penicillin per kilogram of body weight.

Maximum therapeutic results may be expected from dosages in excess of 1,000 units of penicillin per kilogram of body weight. If administered without regard to body weight, maximum therapeutic results may be expected from dosages in excess of 100,000 units of procaine penicillin.

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Uniformity of Kahn Antigen

Mutually Established Criteria for an Acceptable Antigen and the Use of a Reference Antigen by the Michigan Department of Health Laboratories ¹ and the Serology Laboratory of the University of Michigan Hospital ²

Pearl L. Kendrick, Sc. D., and Reuben L. Kahn, Sc. D.

Wherever serologic tests for syphilis are performed, there is the ever present problem of obtaining uniform results, not only within a particular laboratory but also with respect to other laboratories performing similar tests. An attack on this problem as it relates to the United States as a whole has been made by the United States Public Health Service in its annual surveys of the serologic laboratories of State health departments.

In Michigan, collaborative efforts made by the Michigan Department of Health Laboratories and the Serology Laboratory of the University of Michigan Hospital have for many years been directed toward a high level of uniformity of serologic results within the State. To this end, the Michigan Department of Health Laboratories have conducted surveys with check serums and have produced and distributed Kahn antigen for all laboratories registered for the serodiagnosis of syphilis.

Several years ago in Michigan, unusual difficulties with serologic results were

¹ Members of the collaborating group from the Michigan Department of Health Laboratories include: G. D. Cummings, M. D., Director of Laboratories; H. E. Cope, M. D.; Grace Eldering, Sc. D.; M. B. Kurtz, D. V. M.; and Irma Hill, M. S.

² Members of the collaborating group from the Serology Laboratory of the University

of Michigan Hospital include: Elizabeth B. McDermott, Virginia Bradford, and Josephine Baldwin, M. P. H.

³ Chairman, Committee on Serodiagnosis of Syphilis, Michigan Department of Health Laboratories.

⁴ Chief, Serology Laboratory, University of Michigan Hospital.

encountered which led to reconsideration of the various phases of the problem by the Committee on the Serodiagnosis of Syphilis, appointed by the Director of Laboratories in collaboration with the staff of the Serology Laboratory of the University of Michigan Hospital. A series of conferences resulted in recognition of certain mutually acceptable criteria for a Kahn antigen and for the establishment of a reference antigen to be used as a guide in standardizing all antigens for use or distribution by either of the two laboratories or for checking antigens received from other laboratories for study.

In July 1946, a lot of standard Kahn antigen which conformed closely to the accepted criteria was designated as a reference antigen, and a quantity was placed in reserve for use in the standardization of other antigens. A second reference antigen was designated in February 1948; two others are now under study. It is considered important to have several lots of carefully studied reference antigens under constant comparison in order to avoid errors due to an unrecognized change in any one reference antigen. Designation or withdrawal of any particular antigen as a reference lot is done through mutual study and agreement only.

Criteria for an Acceptable Kahn Standard Antigen

In general, an antigen is considered acceptable only when all methods of evaluation yield satisfactory results in comparison with a reference antigen and with accepted standard antigens in current use. More specifically, the criteria established jointly by both laboratories are as follows:

- 1. Titration.—An acceptable antigen should show a sloping titration picture, that is, it should show progressively decreasing turbidity when antigen suspensions in the range from 1+0.8 to 1+1.9 (antigen plus 0.9-percent salt solution) are tested with negative serum and with salt solution. The acceptable titer should be not less than 1+1.1 nor more than 1+1.5 (antigen plus salt solution).
 - 2. Dispersibility.—The aggregates in an

antigen suspension, when prepared at its titer and when prepared by using 0.1 ml. less saline solution than required by the titer of the antigen, should be dispersible in saline solution and in negative scrum, after the suspension has been aged for 30 minutes. Negative serum reactions should be neither cloudy nor too clear, but should be of a degree of opalescence characteristic of Kahn negative reactions.

3. Sensitivity.—The antigen should show the standard degree of sensitivity, as judged by comparison with a reference antigen and with a standard antigen in current use. The antigen should not be markedly affected in sensitivity by an increase or decrease of its titer with the use of 0.1 ml. of saline solution.

Procedure for Testing a New Antigen

Determination of Titer

Table 1 illustrates the titration readings based on dispersibility and turbidity values of suspensions of six different antigens in comparison with a reference antigen. As indicated, the suspensions are prepared by mixing a constant amount of antigen with varying amounts of salt solution in the range from 1+0.8 to 1+1.9. Each mixture is tested with salt solution and serum in the same three ratios as are used in the standard test with serum. The optimum dispersibility (opalescence) of an antigen at its accepted titer is designated as 100, the figures above 100 representing progressively greater turbidity and those below 100, progressively less turbidity.

The most typical titration picture is shown by antigen lot No. 6. Optimum opalescence (the antigen titer) was obtained with a suspension prepared by mixing 1 ml. of antigen and 1.4 ml. of 0.9-percent NaCl solution. The gradual increase or decrease of salt solution in the preparation of the antigen suspension beyond 1.4 ml. results in a corresponding gradual departure from the opalescence at the antigen titer.

In table 1, both antigen lot No. 5 and the reference antigen provide more than one antigen titration point. Thus, antigen lot No. 5 gives a code number of 100 when 1 ml. of antigen is mixed with either 1.2 ml., 1.3 ml., or 1.4 ml. of salt solution. In such instances, sensitivity tests with syphilitic serums determine the titer.

Unsatisfactory titration readings are illustrated with antigen lots Nos. 1, 2, 3, and 4. Antigen lots Nos. 1 and 2 show no titer, lot No. 3 shows a titer followed by a zone of turbidity, and lot No. 4 shows a flat titration.

Determination of Sensitivity

The new lot of antigen should be tested in parallel with the reference antigen and with the antigen in current use, employing as many specimens as possible from the following categories:

- 1. Individual weakly positive serums.
- 2. Pooled weakly positive serums.
- 3. Individual positive serums (with the quantitative procedure).
- 4. Serums of known sensitivity stored in "deep freeze" (1).

- 5. Serums from daily routine procedure.
- 6. Positive serums from supposedly nonsyphilitic persons.
- 7. Positive and negative spinal fluids. The sensitivity of a new lot of antigen should be within the sensitivity range of the reference antigen. This is illustrated in tables 2 and 3. It is important that the summations of plus signs be applied only to serums which give broadly comparable results and not to serums with atypical zone reactions.

Performance of Comparative Tests

As an aid to uniformity, the following is to be noted: (1) the serum-antigen mixtures should be allowed to stand from 3 to 7 minutes before shaking; (2) the salt solution should be added to the tubes as nearly simultaneously as possible before the comparative reading of results; and (3) the usual immediate and 15-minute readings should be made.

Table 1.—Antigen titration readings (with numerical key for interpretation)

			111	ustrat	tive tit	ration	readir	ngs			
Antigen lot No.		(1 m	ıl. of a			varyin in mill			of salt	;	Titration result
	0.8	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.9	
					Code	No.					Unsatisfactory
1 2 3	$105 \\ 102 \\ 105$	105 99 103	104 98 102	104 97 101	104 96 100	104 96 101	104 95 102	103 95 103	103 95 104	103 95 104	No titer—too cloudy. No titer—too clear. Titer followed by zone of turbidity.
4	105	103	102	101	101	101	101	101	101	101	"Flat" titration. " Satisfactory
5	105 105	103 104	101 103	$\frac{100}{102}$	1 100 101	100 1 100	99 99	98 98	96 96	95 95	"Sloping" titration. "Sloping" titration.
Reference antigen	105	103	101	100	1 100	99	99	98	96	95	

Key to Code Nos.

105-Cannot be seen through.

104—Much too eloudy. 103—Too cloudy. Aggregates usually nondispersible.1

102—Slightly too cloudy. 101—Trace cloudy—opalescence approaching optimum. ² 100—Opalescence optimum.

-Trace clear—opalescence approaching optimum.

-Slightly too elear. -Too elear.

-Much too clear. -Water clear.

Aggregates usually dispersible.

1 Antigen titer (optimum opalescence).

² Opalescence of 100 is considered optimum; 99 or 101 may be acceptable in certain instances.

Table 2.—Illustrative sensitivity results of a new lot of antigen in standard 3-tube test with weakly positive serums

Judgment on sensitivity of new lot of antigen	Antigen		rence and cu	ncw antigen irrent stand-
o degrada on sensitivity of her lot of antigen	lot No.	New antigen	Reference antigen	Standard antigen in current use
Unsatisfactory	1 2	i 196 290	178 321	165 336
Satisfactory	1 2 3	334 169 111	331 160 115	328 151 109

¹ The figures represent summation of plus signs and include all plus signs less than 4+ and only one of the 4+ reactions shared by all antigens in the comparative tests.

Table 3.—Illustrative sensitivity results of a new lot of antigen in quantitative tests^o with individual serums

		Comparative result	s of new	antigen ard anti		rence an	d current	t stand-
Judgment on sensitivity of new lot of antigen	Antigen lot No.	Antigen			Serum o	lilutions		
		Antigen	1:2	1:4	1:8	1:16	1:32	1:64
Unsatisfactory	2	New	4 4 4 4 4	1 4 4 4 4	- 4 4 4 3 2	1 1 4 1 1	_ _ _ 3 _	- - - - -
Satisfactory	2	New	4 3 2 4 4 4	2 2 1 4 4 4	- - - 4 4 4	- - 2 4 4	- - 1 2 3	-

Retesting of a Newly Standardized Antigen

The antigen should be resampled and retested after approximately 1 month, at which time it can be released for distribution. Each antigen should be resampled and retested at intervals of approximately 6 months.

Comments

For 3 years, the serology laboratories of the Michigan Department of Health and of the University of Michigan have followed the plan for Kahn antigen standardization as herewith outlined. Every antigen produced in either laboratory, released for use or received for testing, has been standardized in accordance with

these mutually established criteria and in relation to the common reference antigen. It is believed that during this period, the degree of uniformity in serologic results attained in these laboratories has been greater than that previously attained and that this collaborative method of antigen standardization has resulted in greater uniformity of reporting serologic findings to physicians.

This paper is in the nature of a progress report. Other problems relating to the production of Kahn antigen and to the uniformity of Kahn test performance are under continuing study.

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Report on the Venereal Disease Control Cost Analysis, Fiscal Year 1948 ¹

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The extensive cost analysis made by District Office representatives of the Division of Venereal Disease in nearly every State, covering expenditures for fiscal year 1945, provided much-needed information concerning the source of funds utilized in the venereal disease control program and concerning the unit costs of its various activities. This information has been used extensively by the Division of Venereal Disease of the Public Health Service and by the several States in the formulation of postwar plans.

The cost data obtained in the 1945 survey were, of course, derived from price levels existing prior to the lifting of wartime controls. The over-all monetary costs have changed materially with rising prices; consequently, it was deemed advisable to determine the effect of the inflationary trend upon both the costs of the various phases of venereal disease control and upon the sources of funds employed in the control program. A second cost survey was therefore made in a modified form during fiscal year 1948 with the principal objectives of: (a) estimating present costs of venereal disease control programs; (b) detecting internal shifts among the various functions; and (c) obtaining more explicit data on the sources of venereal disease control funds than can be obtained through existing budgetary and expenditure reporting. The present survey was carried out by Regional Office representatives of the Division of Venereal Disease, beginning in January 1948.

With the experience and results of the

¹ From the Division of Venereal Disease.

1945 cost analysis as a guide, certain changes were made both in the extent of the study and in the method used. Instead of collecting retrospective percentage estimates of staff time spent on venereal disease control activities from the whole country or even whole States, a more thorough analysis involving an actual time study of staff activities was made in a small number of selected sample counties and cities in 10 States and in two cities in two additional States. It was the aim, with this approach, to secure a more accurate account in the surveyed jurisdictions of the total time and money spent on venereal disease control and a more accurate break-down of the money spent on the various functions performed. The size of the sample was limited by the time and staff which the Regional Offices could make available for the survey.

In the selection of the sample States and counties, use was made again of the results of the 1945 survey. At that time a clear relationship was demonstrated between the population of a State (or county) and its expenditures. For the present study, therefore, the States were grouped, or stratified, according to population, and one or more representative samples were selected from each group. A similar procedure was followed in selecting sample counties within the sample States, with a detailed check to insure the selection of counties that represented a wide range regarding such characteristics as population, urbanization, prevalence of syphilis, organization and extent of control program, and other factors affecting expenditures. Since the most populous county was included in

each State sample, as well as some of the other large counties, the sample represents from 40 to 50 percent of the population and from 35 to 80 percent of the expenditures in the sample States. In a few of the largest cities and in the most populous counties, the sample was further reduced by the selection of sample clinics for survey within the local organization.

In order to secure the best possible estimate for the nonsample areas in each State with a minimum of effort, a very simple form of survey was made of all nonsample counties in the sample States and of all nonsample clinics in the cities or counties surveyed by sampling.

The basic data obtained in the study include:

- 1. An enumeration of staff positions and salaries by source of funds.
- 2. The break-down of each staff member's time for 1 week into the various tasks or functions performed.
- 3. Nonsalary expenditures for 3 months, by object of expenditure and by source of funds.
- 4. Records of activities carried out over a 3-month period.
- 5. For nonsample areas and units, estimates of average weekly time spent on venereal disease control by all staff members.
- 6. Local and State central office expenditures for the 3-month survey period, by function and by source of funds.
- 7. Records pertaining to rapid treatment project funds and to grant-in-aid payments, both available at headquarters.

In estimating State expenditures, the figures by function and by source of funds for each sample county were expanded by the necessary factor to equal the estimated expenditure for the entire stratum, the nonsample expenditure having been arrived at from the simpler survey form used in those areas. The expenditures in the various strata, in the rapid treatment facilities, and in the State's central office were then added to secure the total State estimate.

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The estimate of the total expenditure for all States was based on the relation between population of State and expenditures as found in 1945 and as determined from the 1948 survey results. The total expenditure for rapid treatment projects was then added to the resulting estimate to arrive at the total for all States. Since the characteristics of the various State programs, as well as the distribution of funds from various sources, tend to follow regional patterns, the distributions of expenditures by function and by source of funds were expanded in regional groups of States rather than by population groups. Expenditures by Federal headquarters not assignable to any particular State are not included in the totals shown.

Results

The results of the study are presented in the six accompanying tables, which show annual estimates of expenditures in terms of amount and percentage, by function and by source of funds, for the 10 sample States, New York City, Philadelphia, and the total for all States; unit costs of some of the most important activities performed in the control program; and a comparison of average staff salaries in 1948 with those paid in 1945.

Table 1 shows the total expenditures in the sample States and cities and for all States, by function, along with the 1945 estimates for purposes of comparison. The total expenditure for both outpatient and in-patient programs amounted to \$36,662,000, as compared to \$27,415,000 in 1945. Of the total amount, about \$8,686,000 was devoted to in-patient care, while the remainder of the program cost \$27,976,000. As expected, the table shows a general increase in expenditures for all functions in 1948 as contrasted to 1945.

Comparisons between 1945 and 1948 are facilitated by reference to table 2, which shows the table 1 data on a percentage basis, with absolute and relative changes indicated. This table shows that the increase in total expenditure since 1945 amounted to nearly 34 percent. While the figures for all States in 1948

Table 1.—Estimated * expenditures for venereal disease control in selected sample States and cities and in all States, fiscal year 1948, by function

[Amount of expenditure] 2

		Total	\$1,804,153 \$1564 \$1564 \$256,222 \$256,222 \$444 \$172,202 \$144,905 \$172,202 \$144,905 \$184,905 \$184,905 \$187,202 \$187,202 \$181,905 \$181
	1	гапа О	\$37.0 17.5 17.5 19.18 60.4 60.4 60.4 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2
	Janitor and	nance nance work	\$19, 084 1, 904 3, 220 20, 284 0, 1, 004 3, 840 27, 724 6, 664 6, 664 7, 492 7, 492 5, 256 8, 274, 540
	Medical, epidemi-	control records	\$147, 416 \$9, 184 \$9, 184 \$9, 302 \$14, 392 \$1, 504 \$6, 504 \$1, 504
	Follow-up	cases	\$37, 260 4, 196 4, 196 65, 180 2, 112 4, 640 6, 160 78, 40 6, 160 78, 304 31, 948 969, 341 787, 199
	Investiga-	suspects	\$59,348 50,928 73,548 128,496 14,184 4,495 14,616 0,656 149,936 16,100 16,100 16,100 2,328,058
,	Patient inter-	viewing	\$53, 880 17, 324 15, 032 73, 204 2, 168 1, 816 4, 956 77, 864 17, 864 17, 864 11, 169, 473 1, 169, 473 1, 169, 473
	Labora- tory	services	\$149, 216 80, 492 56, 772 291, 824 35, 656 27, 508 32, 502 43, 776 194, 732 184, 848 417, 732 184, 848 417, 732 184, 848 417, 732 184, 848 417, 596 3, 568, 878
	ent and tation	In- patient 3	\$721, 509 213, 602 213, 602 315, 252 315, 252 316, 252 316, 252 317, 262 13, 945 7, 126 13, 672 248, 755 79, 559 17, 154 98, 4154 98, 4154 8, 686, 389
	Treatment and consultation	Out- patient	\$223, 400 31, 984 51, 120 467, 156 2, 564 22, 376 22, 376 223, 768 184, 660 518, 103, 788 4, 773, 642
	Diagnosis		\$153, 348 34, 700 47, 460 254, 400 9, 336 9, 336 17, 964 307, 756 86, 420 26, 196 3, 987 1, 995, 984
	Adminis-	tration	\$202, 676 28, 344 172, 380 4, 996 2, 052 37, 112 23, 684 85, 092 85, 092 85, 092 87, 740 27, 524 87, 524 87, 524
	Arca		Georgia Kentucky California California Idaho Utah Kansas Wisconsin Ohio New Jersey New York City Philadelphia All States, 1945

¹ Estimates based on a 3-month survey and on a 1-week time study in selected sample counties and cities.

 2 Figures have been carried to the nearest dollar for convenience, although the estimates are not assumed to possess that degree of accuracy. 3 Not estimated from a sample but derived from complete accounting of rapid treat-

ment projects.

4 Excluding Federal administrative and other expenditures not assignable to any particular State, and excluding expenditures in the Territories.

⁵ Estimated, since "administration and maintenance" was treated as a single category in the 1945 survey.
⁶ Estimated, since no comparable figure is available for 1945.

Source: Forms PHS-431 (VD) to PHS-433 (VD), inclusive; annual report of rapid treatment center expenditures; and report of 1945 cost analysis, FSA-PHS-VD Division.

Table 2.—Estimated * expenditures for venereal disease control in selected sample States and cities and in all States, fiscal year 1948, by function

[Percent of expenditure]

Area	Adminis-	Diagnosis	Treatment and tation	Treatment and consul- tation	Laboratory	Patient inter-	Investi-	Follow- up of	Medical, epi- demiologic,	Ja		i de
	tration		Out-patient In-patient	In-patient	services	viewing	suspects	lapsed	and control rccords	nance work	- College	Lovai
Georgia	11.0	8, 4	12.1	41.2	8.1		3.2	2.0	8.0	1.1		100.0
Kentucky	4.5. 4.4	9.0	6.1	40.6	15.3		9.7	.04	11.2	4.	1.4	100.0
California	7.9	11.7	21.5	14.6	13.4		10.00 0.00	3.0	14.5	0.0.		100.0
Idaho.	93.7	9.4	1.9	36.8	26.5	1.6	9.0	4.0	100	0.	4.7	100.0
Kansas	15.1	14.4	21.8	9.61	13.2		တ ကို ဟု	. i. e.	14.5	1.6	. എ . ജ	100.0
Wisconsin.	12.4	9.4	11.6	7.1	22.8		3.2	3.2	10.0	.2	17.5	100.0
Ohio	8.4	17.5	13.3	14.1	11.2		တ်	4.5	17.1	1.6	3.0	100.0
New York City	0 C	0.01	25.3	e, ∝ 21 π.	21.2		- òx	ე დ 4- დ	13,2	×. 4	77 7	0.00
Philadelphia	5.2	14.2	19.7	18.7	6.2		3.1	6.1	17.7	1.0	4.3	100.0
All States, 2 1948.	8.7	10.9	13.8	23.7	14.0	3.2	7.1		12.0	6.		100.0
All States, 1945	39.6	7.3	17.4	4 23.5	13.3	4.0	8.5	2.9	9.6	31.0	2.9	100.0
Change, 1948/1945	5+20.1	+99.8	+6.3	4+35.0	+41.0	+7.4	+10.9	+23.1	+68.1	5+20.1	+38.8	+33.7
Relative change, 1948/1945	5-10.2	+49.4	-20.5	++ 0	+5.4	-19.7	-17.1	-7.9	+25.7	5-10.2	+3.8	0.0
Tectimotoc honord on to 2 month assumers as 1 mg			1 2 2	1	F			9				

1 Estimates based on a 3-month survey and on a 1-week time study in selected sample

counties and cities.

2 Excluding Federal administrative and other expenditures not assignable to any particular State, and excluding expenditures in Territorics.

2 Estimated, since "administration and maintenance" was treated as a single category in the 1945 survey.

⁴ Estimated, since no comparable figure is available for 1945.
⁵ The percentage changes in columns 1 and 10 agree exactly only because of the method of estimating. See footnote 3 above.

Source: Table 1, p. 110.

Table 3.—Estimated 'expenditures for venereal disease control in selected sample States and cities and in all States, fiscal year 1948, by source of funds

[Amount of expenditure] 2

		Federal grants	grants			Non-Federal sources	al sourees		
Агеа	Rapid treatment project 3	Formula 4	Other Federal	Total	State	Local	Other	Total	All sourees
Georgia	\$485,041			ł	\$473,382	\$445, 129	\$14,387		
Kentueky	165,770	268, 939	23, 471	458, 180	19, 201	48,841	0	68,042	526, 222
Oklahoma	109, 761			_	142, 109	98,618	10, 222		-
Callioruia	35 576				27, 227	13, 670	112		
Itah	11, 725			_	21, 957	7,612	0		
Kansas	4,362				65, 888	65, 089	1, 599		
Wiseonsin	9,151				63, 615	40, 722	0		
Ohio	171,018				50, 484	1, 072, 392	137, 788		_
New Jersey	50,772				99, 750	502, 217	48, 131		866,
New York City	90,804				0	1, 705, 120	206, 370		
Philadelphia	68, 106				278	224, 227	51, 204		
All States 6	6, 158, 271	8, 068, 587	1,198,117	15, 424, 975	5, 506, 415	14, 485, 130	1,245,273	21, 236, 818	36, 661, 793
		5			-				

 $^{\rm 1}$ Estimates based on a 3-month survey and on a 1-week time study in selected sample counties and cities. $^{\rm 2}$ Figures have been carried to the nearest dollar for convenience, although the estimates

are not assumed to possess that degree of accuracy.

³ Not estimated from a sample but derived from complete accounting of rapid treatment projects.

 4 Estimates from sample corrected to agree with record of payments and uncncumbered balances of grant-in-aid funds.

⁵ Excluding Federal administrative and other expenditures not assignable to any particular State, and excluding expenditures in the Territories.

Source: Forms PHS-431 (VD) to PHS-433 (VD), inclusive; "Rapid Treatment Center Expenditures by Source of Funds," fiscal year 1948, FSA-PHS, Division of Venercal Disease; "Grant-in-Aid Payments to States," fiscal year 1948, FSA-PHS, Burcau of State Services.

and 1945 do not appear to indicate great variation from function to function, a different impression is gained from the last two lines of table 2, where the changes from 1945 to 1948 are shown on a percentage basis, plus or minus. noted in table 1, the absolute changes are plus for all functions. The last line of table 2, however, shows the percentage change in each function relative to the change in the total; i. e., those functions that increased proportionately more than the total appear as pluses, while those that increased proportionately less than the total appear as minuses. This line reveals significant changes in a number of functions. The relative expenditures for diagnosis, for example, increased by nearly half; the relative expenditures for in-patient treatment remained practically stationary; while those for outpatient treatment decreased by 20 percent. Other changes that appear worthy of note include a 26-percent relative increase in expenditures for record keeping and relative decreases in expenditures for patient interviewing (20 percent) and for the investigation of suspects (17 percent).

Table 3 shows the distribution of expenditures by source of funds for the

sample States and cities and for all States. The total of Federal funds expended amounts to \$15,425,000, while \$21,237,000 was contributed by non-Federal sources. The Federal funds consisted of a little over \$6,000,000 to rapid treatment projects, a little over \$8,000,-000 to grants-in-aid, and about \$1,200,000 from other Federal sources. Of the non-Federal funds, the States contributed \$5,500,000 and the local governments slightly under \$14,500,000, while \$1,245,-000 was contributed by miscellaneous other sources.

Table 4 shows the percentage distribution of funds from the various sources and reveals that Federal grants amounted to 42 percent of the total, while non-Federal sources contributed about 58 percent. Federal contributions to the 10 sample States range from 25 percent in New Jersey to 87 percent in Kentucky.

Table 5 summarizes the unit costs and the median unit costs in nine sample States. No attempt was made, because of the small size of the sample, to arrive at average unit costs for the entire country.

The extent to which rising costs since 1945 have affected the program may be

Table 4.—Estimated ¹ expenditures for venereal disease control in selected sample States and cities and in all States, fiscal year 1948, by source of funds

[Percent of expenditure]

		Federal	grants		Non-Federal sources				
Area	Rapid treatment project	Form- ula	Other Fed- eral	Total	State	Local	Other	Total	All sources
Georgia_ Kentucky_ Oklahoma California_ Idaho_ Utah_ Kansas Wisconsin_ Ohio_ New Jersey New York City_ Philadelphia_ All States 2_	26. 9 31. 5 20. 2 10. 0 26. 4 15. 0 1. 8 4. 8 9. 7 5. 9 4. 4 12. 9	20. 2 51. 1 29. 0 17. 1 24. 3 44. 7 29. 4 40. 2 15. 4 15. 7 1. 9 24. 1	1. 2 4. 5 4. 6 1. 4 18. 9 2. 5 16. 2 . 6 3. 3 3. 4 . 4 10. 6	48. 3 87. 1 53. 8 28. 5 69. 6 62. 2 47. 4 45. 6 28. 4 25. 0 6. 7 47. 6	26. 2 3. 6 26. 2 16. 1 20. 1 28. 1 26. 8 33. 2 2. 9 11. 5 .0 .1	24. 7 9. 3 18. 1 53. 7 10. 2 9. 7 25. 2 21. 2 60. 9 58. 0 83. 2 42. 6	0.8 .0 1.9 1.7 .1 .0 .6 .0 7.8 5.5 10.1 9.7	51. 7 12. 9 46. 2 71. 5 30. 4 37. 8 52. 6 54. 4 71. 6 75. 0 93. 3 52. 4	100. 0 100. 0 100. 0 100. 0 100. 0 100. 0 100. 0 100. 0 100. 0 100. 0

¹ Estimates based on a 3-month survey and on a 1-week time study in selected sample counties and cities.

Source: Table 3, p. 112.

² Excluding Federal administrative and other expenditures not assignable to any particular State and excluding expenditures in the Territories.

estimated by a comparison of the unit costs and of the salary rates shown in two of the tables. Table 5 gives unit costs for nine sample States in 1948 and the corresponding figures for 1945, as well as the median values for these States for both years. This table shows that unit costs increased in nearly all instances during the 3-year period. The median values for the sample States increased from 34 to 175 percent.

Table 6 presents average salary rates paid to staff members in six widely scattered cities for which comparable data were available for 1948 and 1945. These figures throw additional light on the general increase in expenditures described

above. The only decreases seen to have occurred are physicians' salaries in Oklahoma City and Milwaukee, while clerical salaries in Oklahoma City remained unchanged. In all other instances the salaries increased, the 1948 rates running as high as 99 percent above those paid in In the cities compared, average salary increases amounted to 40 percent for physicians, 27 percent for nurses and investigators, and 19 percent for clerical workers. Since these figures are based on only six cities, they may not be regarded as reliable averages for the entire country, but merely as indicative of the trend and of the variations to be found from place to place.

Table 5.—Unit costs of venereal disease control activities in selected sample States, 1948 and 1945

		Clini	c cost	Clinic cost of out-	Total interview cost per contact named 2	Cost of investiga-		Cost of follow- up	
State	Year	Per diag- nos- tic ob- serva- tion	Per infect- ed case diag- nosed	patient treat- ment per treat- ment visit 1		Per suspect investi- gated	Per new case dis- covered by inves- tigation	Per lapsed case in- vesti- gated	Per case re- turned to treat- ment
Georgia	1948 1945	\$1.13 .50	\$5, 80 2, 66	\$2. 59 . 42	\$2.14	\$3. 43 2. 30	\$16, 62 11, 73	\$9.11 .25	\$12. 22 1.07
Kentucky	1948 1945	.76	2. 60 3. 87	. 68 . 56	2. 28	2. 92 4. 45	10. 18 15. 22	3.00	5. 49
Oklahoma	1948 1945	1, 19 1, 32	5. 08 2. 84	2. 09 . 52	1.55	4, 63 2, 17	10. 65 7. 79	1.75	2. 64
California	1948 1945	3.00	10. 51 4. 74	1. 28 . 61	7. 36	3. 80 2. 60	11. 58 10. 68	3. 01 12. 39	5. 48 35. 27
Idaho	1948 1945	1. 53	40, 39 8, 01	14, 85 1, 33	³ 18. 91	29. 83	³ 142. 50	5. 69	41.67
Utah	1948 1945	1. 72	6. 97 4. 13	2. 58 1. 28	4. 83	15, 35 2, 78	³ 30. 00 7. 47	14. 77 3. 55	14. 77 8. 58
Kansas.	1948 1945	3. 61	14. 36 5. 41	1. 62	1. 67	4. 16 2. 01	16. 67 7. 39		
Ohio	1948 1945	1.17 .70	5. 52 2. 71	. 45 . 46	4.06	6. 35 1. 37	12. 76 6. 51	1.86 1.70	2. 49 2. 11
New Jersey	1948 1945	1. 08 1. 07	6. 88 4. 72	1, 10 . 81	1. 94	4.06 3.82	21. 65 8. 47	4. 44 2. 17	6, 80 3, 18
Median	1948 1945	1. 19 . 89	6. 88 4. 13	1. 62 . 59	2. 28	4. 16 2. 45	16. 62 8. 13	4. 44 2. 59	6. 80 4. 34
Percent increase in the median cost in 1948_		33. 7	66. 6	174. 6		69. 8	104. 4	71. 4	56. 7

¹A major factor in the increased cost per treatment visit since 1945 has been the introduction of penicillin, which is considerably more expensive than the drugs which it supplanted.

³ Based on fewer than 25 cases.

Source: Computed from forms PHS-431 (VD) to PHS-433 (VD); 1945 cost analysis, FSA-PHS-VD, 7-31-46.

² Data for 1945 and 1948 are not comparable as regards contact interviewing. The 1948 figures are based on the cost of all interviewing and therefore exaggerate the cost of interviewing for contacts.

Table 6.—Comparison 1 of hourly salary rates in venereal disease control in 6 cities, 1948 and 1945

Position and city	1945	1948	Percent change, 1948/1945
Physicians:			
Atlanta	\$3,43	\$5,18	+51
Oklahoma City	2, 89	2, 75	-5
San Francisco	2. 32	3, 21	+38
Milwaukee	2,80	2.44	-13
Dayton.	2.17	4. 24	+95
Newark	2. 20	4.38	+99
Mean of cities listed	2.64	3.70	+40
Nurses and investigators:			
Atlanta	. 72	. 76	+6
Oklahoma City	.95	. 98	+3
San Francisco	1.08	1.50	+39
Milwaukee	. 97	1. 25	+29
Dayton	1.08	1, 27	+17
Newark	. 85	1.39	+64
Mean of cities listed	. 94	1.19	+27
Clerical workers:			
Atlanta	. 70	. 76	+9
Oklahoma City	.78	. 78	0
San Francisco	. 87	1.06	+22
Milwaukee	. 89	. 95	+7
Dayton	. 69	. 99	+43
Newark	. 69	. 97	+41
Mean of cities listed	. 77	. 92	+19

¹ Based on average salaries paid to staff members in out-patient clinical work, case finding, and case holding (excluding those central office staff members whose salaries were not reported individually).

Source: Form PHS-431 (VD), 1948; forms 1 and 2, 1945 cost analysis.

Summary

A survey of expenditures for venereal disease control was made during fiscal year 1948, based on a 3-month survey and a 1-week time study in sample areas in 10 States and in New York City and Philadelphia. Data were analyzed to reveal expenditures by function and by source of funds. Unit costs of important activities in the program were determined. In six cities the average staff salaries for 1948 were compared with those paid in 1945.

Results are presented in the form of six tables showing the above-mentioned analyses for each State and city surveyed and for the entire country. Salient features of the findings include the following:

- 1. Expenditures increased about 34 percent, from \$27,415,000 in 1945 to \$36.662.000 in 1948.
- 2. Expenditures for all functions increased between 1945 and 1948 as regards absolute amount. On a percentage basis

relative to the change in the total, however, both increases and decreases are revealed in the expenditures, by function: sizable relative increases occurred for diagnosis and record keeping, and appreciable decreases occurred for outpatient treatment, patient interviewing, and the investigation of suspects.

- 3. The Federal contribution to the program amounted to \$15,425,000, or 42 percent of the total. Federal contributions in the sample States ranged from 25 to 87 percent.
- 4. Unit costs of control activities exhibit almost universal increases over the 1945 figures. Median values of unit costs for the States surveyed increased from 34 to 175 percent.
- 5. Salary rates for staff were compared for six widely separated cities. These rates have increased in nearly all instances since 1945. Average increases in the six cities amounted to 40 percent for physicians, 27 percent for nurses and investigators, and 19 percent for clerical workers.

CURRENT NOTES AND REPORTS

Announcement

On April 27–28, 1950, there will be held in Washington, D. C., a meeting on venereal disease research sponsored jointly by the American Venereal Disease Association and the Experimental Therapeutics Study Section, National Institutes of Health, Public Health Service, Federal Security Agency.

The first day, Thursday, April 27, will be devoted to papers on *Treponema pallidum*, experimental syphilis, early syphilis, other venereal diseases, and the newer antibiotics in syphilis.

The business meeting of the American Venereal Disease Association (limited to members) will be held on Friday morning, and papers will be presented on neurosyphilis and miscellaneous aspects of syphilis. In the afternoon session there will be a panel discussion on the international aspects of venereal disease control, and papers will be presented on the treponemal immobilization tests and on the epidemiology and serology of syphilis.

The program for each day will be held in the Thomas Jefferson Auditorium, United States Department of Agriculture, Fourteenth Street and Independence Avenue SW., beginning at 10 a. m.

All persons interested in venereal disease are cordially invited to attend the meeting. Copies of the program will be sent at a later date upon request.

Inquiries should be addressed to: Mr. Francis L. Sehmehl, Executive Secretary, Experimental Therapeutics Study Section, Division of Research Grants and Fellowships, National Institutes of Health, Bethesda 14, Md., or to Dr. William L. Fleming, Secretary, American Venereal Disease Association, 750 Harrison Avenue, Boston, Mass.

Harvest Camps in New York State Get VD Surveys

The New York State Department of Health Bulletin for January 2 reports on venereal disease surveys conducted in farm and labor camps during the past harvesting season. Camps selected for the surveys were those in which, on the basis of past experience, 15 or more persons with syphilis would be found.

Treatment with delayed-absorption penicillin was provided for all eases of syphilis not giving a history of prior penicillin therapy and for all patients reporting with clinical evidence of gonorrhea.

Of the 3,610 persons examined, 407 were given treatment. Dosage sehedules shorter than those formerly used allowed a larger number of patients to finish treatment than in previous years. Although twice as many migrant workers were examined in 1949 as in 1944, the number of venereal disease eases found and treated in 1949 was only a little over half the number found and treated in 1944.

The Arkansas Seminar Plan

To reach its greatest effect, a local venereal disease case-finding project must have the cooperation of community leaders. The "Arkansas Seminar Plan" is a program designed with a view to obtaining that cooperation.

The immediate concern of the Arkansas State Board of Health, Venereal Disease Control Division, was the number of congenital syphilis cases uncovered by the Delta Plantation Survey. Ways of teaching the facts of venereal disease to the Arkansas Negro were apparently needed. The seminar plan seemed the most practical means of reaching the Negro community with publicity in advance of a mass blood-testing operation.

Pine Bluff, in Jefferson County, has a high syphilis rate and a large Negro population, making it an obvious place to try the plan. Jefferson County Negro teachers were mailed a series of four letters on consecutive days beginning a week before the scheduled dates of the seminar. Five questions about syphilis were asked in each letter. Answers were given during the seminar.

Information about many of the phases of venereal disease was presented in lectures, films, radio transcriptions, pamphlets, and posters. Question periods followed the lectures, and teachers were asked to submit written questions to a speaker who answered them in simple, factual language.

In order to evaluate the effectiveness of the seminar, at least as to the amount of venereal disease information retained, a true-false and completion-type test was given prior to the lectures. At the end of the seminar, the same test was again used. The marks on the second test were gratifyingly higher,

Although the first seminar covered $2\frac{1}{2}$ days, experience showed that a $1\frac{1}{2}$ -day schedule was equally satisfactory.

Public response to the blood-testing surveys which followed indicated that the seminars had, indeed, produced the desired effect.

VD Radio Documentary Praised as Part of Community Action

Praise for a radio documentary on venereal disease and a discussion of the criteria by which it was judged were contained in an article by Saul Carson, Founding Member of the Radio-Television Critics Circle, in the November-December 1949 issue of the Service Bulletin of the Federal Radio Education Committee.

"Of an even half-dozen broad-canvas shows done on three of the networks in the last year (1948)," said Mr. Carson, "only one seems to this scorekeeper to have met all the qualifications of the good documentary. The program was 'V. D., a Conspiracy of Silence,' written by Erik Barnouw and directed by Martin Andrews" (ABC network on April 29, 1948).

In discussing his criteria for the evaluation of a documentary radio program, Mr. Carson said:

"1. 'V, D.' had something important to say.

"2. It was done with the help of the United States Public Health Service as part of a broad educational campaign; the factual material was accurate and the sociological direction was clear.

"3. The writer was chosen for his competence, not for his bias, and was given the widest latitude artistically. The entire production, from casting to airing, was on a high level of professional competence.

"4. It was fair to its basic subject. (No matter what the medium, whether it is painting or film, fairness and honesty must be among the artist's tools; but in broadcasting there is a specific, extremely compelling reason why fairness must be observed: the law of the

land happens to demand it. Like the West Pointer, radio *must* be a gentle-man—by Act of Congress.)

"5. It prescribed a course of action in definite terms.

"6. In recognition of the limitations of radio's 'one-shot broadcasts,' it did not depend for its impact solely upon a single program, but was part of a large, well-organized campaign extending into the entire community.

"7. It was broadcast at peak time.

"You will note," Mr. Carson continued, "that the program 'V. D.' was part of a large campaign being conducted by a Government agency against the 'conspiracy of silence.' Barnouw's show was not

only the opening gun of that campaign, it set standards for the campaign itself; never before had the subject of venereal disease been discussed with such candor on a network. Furthermore, the Barnouw piece (as noted in point 6, above) acknowledged that by itself it could accomplish very little. Public action would result not from the broadcast of a 'oneshot' radio documentary, no matter how competently executed, but from the wide use of radio and other media of mass communication. The 'V. D.' documentary, its artistic integrity granted, had what is much more immediately, directly, and recognizably important to us-absolute meaningful social integration."

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CURRENT LITERATURE

ACTA DERMAT.-VENEREOL., (SUPPLEMENT), HELSINKI

Investigation of 120 children born of mothers infected with lymphogranuloma inguinale. C. E. Sonck. Acta dermat.-venereol., 29: 3-61, 1949. (Supplement 23.)

None of the children examined, who were born of mothers in the acute or chronic phase of infection, of mothers symptom-free (treated), or born after healed bubo inguinalis, showed any symptoms of lymphogranuloma venereum. Of 90 Frei tests given, 88 were negative. In one case an indefinite reaction was obtained. One child, of eight not included in the above grouping, showed lymphogranuloma venereum with positive Frei reaction.

AM. HEART J., ST. LOUIS

Calcification as a diagnostic sign of syphilitic aortitis. M. C. Thorner, R. A. Carter, and George C. Griffith. Original Communications. Am. Heart J., 38:641-653, Nov. 1949.

During a 9-month period 38 cases of syphilitic acrtitis were studied at the

Los Angeles County General Hospital, 19 showing calcification of the thoracic aorta and 15 of the ascending aorta.

Linear calcification of the ascending aorta is a valuable sign in syphilitic aortitis.

AM. J. M. TECHNOL., HOUSTON

The serology of syphilis with special reference to cardiolipin and Kolmer antigens. John A. Kolmer. Am. J. M. Technol., 15: 293-298, Nov. 1949.

A detailed review, presented before the Pennsylvania Society of Medical Technologists and Laboratory Technicians, Philadelphia, April 23, 1949, goes back to the time of Pangborn, who isolated the cardiolipin antigen.

AM. J. OBST. & GYNEC., ST. LOUIS

Surgical treatment of sterility. Robert N. Rutherford, Howard M. Lamborn, and A. Lawrence Banks. Am. J. Obst. & Gynec., 58: 673–683, Oct. 1949.

Operative technic in 43 cases of primary and secondary sterility unrelieved by pressure methods is described.

A case report of a 33-year-old house-

wife with a 16-year history of gonorrhea is included. Surgery relieved the fimbrial occlusion. Pregnancy occurred 11 months later.

AM, J. OPHTH., CHICAGO

The diagnosis and treatment of ocular allergy. Alan C. Woods, Am. J. Ophth., 32:1457-1478, Nov. 1949.

Tests are made with gonococci vaccines of various types to obtain an anaphylactic type of reaction. That type from which the patient obtains the greatest reaction is administered via subcutaneous injection as therapy for nongranulomatous iritis (recurrent).

The ophthalmoscopic evaluation of optic atrophy. Alfred Kant. Am. J. Ophth., 32:1479-1486, Nov. 1949.

A study was made of 125 eyes, 49 normal and 76 atrophic, 3 of which were due to syphilis. The number of capillary vessels on the disc was counted according to the Kestenbaum capillary number test in correlation with the visual acuity and area of field determination, the technic serving as a good diagnostic aid.

Healed luctic neuroretinitis papulosa. Paul G. Wolff. Am. J. Ophth., 32:1599, Nov. 1949.

A 28-year-old woman with secondary syphilis revealed poor vision of the right eye of 1 year's duration. Continuous treatment has arrested the progress of the condition,

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

Effects of chloramphenicol in early syphilis. Raymond C. V. Robinson, Lay Martin Fox, and Robert C. Duvall. Am. J. Syph., Gonor. & Ven. Dis., 33:509-514, Nov. · 1949.

A study was made of 17 patients with primary or secondary syphilis treated with chloramphenicol at the Baltimore Rapid Treatment Center. A total dosage of 40 gm. was given over a 10-day period. Maximum time required for lesions to become darkfield negative was 50 hours.

It appeared that chloramphenicol could be treponemostatic rather than treponemicidal,

Penicillin in oil with aluminum monostearate: Its effect on prolonging blood concentrations of penicillin and a preliminary report of its use in the treatment of syphilis. S. R. Taggart, F. D. Hendricks, V. L. Chandler, Henry Welch, D. H. Harley, and S. Olansky. Am. J. Syph., Gonor. & Ven. Dis., 33:515-522, Nov. 1949.

Patients from the venereal disease wards of Gallinger Municipal Hospital, Washington, D. C., were given varying doses of procaine penicillin G in oil with 2 percent aluminum monostearate, using both micronized and nonmicronized preparations. Results are presented for 97 patients.

Experiences with single and multiple treatment schedules of early syphilis with procaine penicillin in oil and aluminum monostearate. Evan W. Thomas, Charles R. Rein, and Delmas K. Kitchen. Am. J. Syph.. Gonor. & Ven. Dis., 33: 523-526, Nov. 1949.

A study of 160 patients treated at Bellevue Hospital, New York City, according to four schedules, utilizing both single and multiple injections, showed excellent clinical and serologic results. The incidence of allergic reactions was low.

Neurosyphilis III. Evaluation after three years of treatment with penicillin alone and with a combination of penicillin and malaria. Arthur C. Curtis, William T. Kruse, and Dorothy H. Norton. Am, J. Syph., Gonor. & Ven. Dis., 33: 527-536, Nov. 1949.

This study was based on the follow-up of 380 patients with various types of neurosyphilis treated at the University Hospital, Ann Arbor, Mich., since 1944. A total dosage of 4,000,000 units of aqueous penicillin was given, and when fever was given concurrently with penicillin, therapeutic tertian malaria was induced. The clinical failure rate was 6 percent with either type of therapy. Patients responded equally well to penicillin alone and to penicillin plus malaria.

Effect of five years of penicillin alone on neurosyphilis. Including some comparisons with prepenicillin methods. John H. Stokes, Mortimer S. Falk, and George D. Gaumon. Am. J. Syph., Gonor. & Ven. Dis., 33: 537-560, Nov. 1949.

A report is presented of the fifth year of experience of the Penicillin-Syphilis Panel of the University of Pennsylvania, The authors conclude that there is hope for arrest by penicillin in any phase of neurosyphilis. A number of charts and graphs are presented.

Penicillin therapy in asymptomatic neurosyphilis. A comparison of the effects of amorphous penicillin, penicillin in oil and wax, and crystalline penicillin G. Fenwick T. Nichols, Jr., and Albert Heyman. Am. J. Syph., Gonor. & Ven. Dis., 33: 561-570, Nov. 1949.

A report is presented of spinal fluid changes in 298 patients with early and late asymptomatic neurosyphilis treated in Atlanta, Ga., since 1944. Tables show relation of total dosage and type of penicillin to spinal fluid responses. Only 10.1 percent of the patients were considered definite treatment failures.

Penicillin failures in neurosyphilis. Bernhard Dattner. Am. J. Syph., Gonor. & Ven. Dis., 33: 571-575, Nov. 1949.

Of 388 patients with various forms of neurosyphilis treated at the Bellevue Hospital, New York City, within the past 5 years, only 43 failed to respond to the first course of intramuscular penicillin injections, varying in amounts from 2 to 9 million units. Of these 43, 24 responded favorably to a second course, usually given in higher amounts than the first one.

The new threshold in venereal disease control. J. R. Heller, Jr. Am. J. Syph., Gonor. & Ven. Dis., 33: 576-578, Nov. 1949.

A summary is given of diagnostic and therapeutic advances in venereal disease control and of unsolved problems in the biology of syphilis.

The frequency of discovery of syphilis in up-State New York between 1936 and 1943. William H. Haenszel and James H. Lade. Am. J. Syph., Gonor. & Ven. Dis., 33:579-586, Nov. 1949.

By collating case reports with serologic survey material, it was found that 41.6 percent of men, 18 through 34 years, found to have positive serologic reactions in selective-service examinations, had been reported previously as cases of syphilis.

The use of cardiolipin lecithin in the preparation of antigen for the Hinton test. William A. Hinton, Genevicvo O. Stuart, and James F. Grant. Am. J. Syph., Gonor. & Ven. Dis., 33:587-592, Nov. 1949.

From a total of 16,205 serologic tests performed, excellent results were obtained by employing the cardiolipin-lecithin indicator in the Hinton test. This made the test extremely high in sensitivity and specificity.

Oral aureomycin in the therapy of granuloma inguinale. Robert B. Greenblatt, Virgene S. Wammock, Robert M. West, Robert B. Dienst, and Calvin H. Chen. Am. J. Syph., Gonor. & Ven. Dis., 33:593-598, Nov. 1949.

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Excellent results were obtained with 16 patients treated at the University of Georgia with doses varying from 10.8 to 70.0 gm. All lesions were healed in an average of 11 days after completion of therapy.

AM. PRACT., PHILADELPHIA

Classification of the rheumatic diseases. With special emphasis on the diagnosis and treatment of rheumatoid arthritis. Stacy R. Mcttier. Am. Pract., 4:196-200, Dec. 1949.

Included is a review of recent contributions on arthritis with a revised classification and differentiation of joint diseases adopted by the American Rheumatism Association. Mention is made of gonorrheal arthritis and arthritis of syphilitic origin (Charcot's joint). General medical management of this condition is stressed.

Arch. Dermat. & Syph., Chicago

Treatment of syphilis with penicillin injection in oil and wax U. S. P. John E. Rauschkolb and Harold N. Cole. Arch. Dermat. & Syph., 60:'676-689, Nov. 1949.

A study of 116 patients with primary and secondary syphilis or early latent syphilis treated with a total of 4,800,000 units of penicillin in oil and wax was made at the Cleveland City Hospital between February and October 1946. Relapse or reinfection occurred in 36 (31.03 percent) of the patients.

Reinfection and relapse after treatment of early syphilis with penicillin. Analysis of one hundred and thirty-seven cases of "infectious failure" in a total series of 1,105 cases. Arthur G. Schoch and Lee J. Alexander. Arch. Dermat. & Syph., 60: 690–700, Nov. 1949.

A study comprising 1,105 patients with primary or secondary syphilis treated with penicillin by five different treatment schedules was made at the Dallas Syphilis and Venereal Disease Clinic during 3½ years, with observation periods ranging from 9 months to 3½ years, for the purpose of differentiating between reinfection and relapse. Of 137 patients who later exhibited evidence of infectious relapse, 80 were diagnosed as reinfections, while 57 were left in the category of infectious relapses.

Pain in a breast due to neurosyphilis. Carl F. Baumeister, Victor P. Slepikas, and Duane D. Darling. Arch. Dermat. & Syph., 60: 1203-1204, Dec. 1949.

The case, believed to be the first of its kind recorded, was a 55-year-old woman who had increasing pain in the right breast for 5 years. Injections of iodobismital brought definite diminution of pain within 3 weeks.

Penicillin-resistant early syphilis. Report of a case. Louis Wexler, Robert N. Bugg, Herbert V. Adams, and Allen D. Smith. Arch. Dermat. & Syph., 60: 1207-1208, Dec. 1949.

The case was a 24-year-old Negro, admitted to the Oliver General Hospital, Augusta, Ga., with the diagnosis of early syphilis, who, after receiving 8,000,000 units of penicillin, developed sccondary syphilis. He responded favorably to heavy metal therapy.

ARCH. NEUROL. & PSYCHIAT., CHICAGO

Chronic pachymeningitis. Report of a case and review of the literature. Howard C. Naffziger and W. Eugene Stern. Arch. Neurol. & Psychiat., 62: 383-411, Oct. 1949.

A description of the pathology of syphilis as the cause of dural changes is included.

ARCH. OPHTH., CHICAGO

Embryonal cataract associated with interstitial keratitis and syphilitic choroiditis. Emanuel Rosen. Arch. Ophth., 42: 749-754, Dec. 1949.

Occurrence of embryonal cataract associated with interstitial keratitis and syphilitic choroiditis is extremely rare. A case is presented of a woman with poor vision, diagnosed after the age of 16 as interstitial keratitis. She observed that her ocular condition became worse during adolescence and menopause.

BRIT. M. J., LONDON

Aureomycin: A new treatment for syphilis?
 R. R. Willcox. Brit. M. J., No. 4636:
 1076-1077, Nov. 12, 1949.

Nine African Negro patients were treated orally with aureomycin in doses of 750 to 1,500 mg. over a period of 24 to 48 hours. In all, darkfields were negative within 48 hours.

CANAD, M. A. J., MONTREAL

Findings in wartime physical examination of volunteers for Air Force service and some implications for the future. (V. D.) A. H. Sellers, A. A. G. Corbet, J. B. Hardie, and G. D. Manderson. Canad. M. A. J., 61: 463-468, Nov. 1949.

Disqualifying defects, including venereal diseases, are listed for candidates for Air Force service.

INTERNAT. DIGEST OF HEALTH LEGISLA-TION, (WHO), GENEVA

Canada 2: British Columbia. Act: Control of venereal diseases. Internat. Digest of Health Legislation, (WHO), 1:158-163, 1949.

A digest of the act for suppression of venereal diseases assented to on April 3, 1947. The Venereal Diseases Suppression Act and the Venereal Diseases Suppression Act Amendment Act, 1938, were repealed.

Denmark 1. Act: Control of venereal diseases. Internat. Digest of Health Legislation, (WHO), 1:190-198, 1949.

Act No. 193 of June 4, 1947, is discussed,

France 1. Decree: Health register of prostitutes. Internat. Digest of Health Legislation (WHO), 1:225-226, 1949.

Decree No. 47–2253 of November 5, 1947 in application of Act No. 46–795 of April 24, 1946 for establishment of a social and health register of prostitutes is discussed.

Hungary 1. Ordinance: Penicillin therapy of gonorrhea. Internat. Digest of Health Legislation (WHO), 1:234, 1949.

The rules set forth in Ordinance No. 191,600/1947 N. M. of the Minister of Social Welfare are reproduced.

J. A. M. A., CHICAGO

Aureomycin and its effects in early stages of syphilis. A preliminary report. Jack Rodriquez, Frederick Plotke, Seymour Weinstein, and William W. Harris. J. A. M. A., 141: 771-772, Nov. 12, 1949.

A study of aureomycin in early infectious darkfield-positive syphilis was made on 27 patients at the Chicago Intensive Treatment Center. With a total oral dosage of 70 gm. given over a period of approximately 11 days, an initial satisfactory decline in serologic titer was obtained, and spirochetes were eradicated from darkfield-positive lesions in an average time of 39 hours. A mild to moderate degree of gastrointestinal disturbance was manifested in almost 100 percent of the patients.

J. AM. DENT. A., CHICAGO

Rapid dental surveys: a case finding procedure for congenital syphilis. Frank P. Bertram. J. Am. Dent. A., 40:45-49, Jan. 1950.

Dentists are key men in the venereal disease control program in checking dental anomalies and Hutchinson's teeth, occurring in sufficient frequency among groups of high incidence to be an effective case-finding adjunct.

The study consisted of dental inspections, at the rate of 100 per hour, of 2,156 Negro school children. Sixty-nine were diagnosed as having Hutchinson's teeth. Fifty-three blood tests were made, 13 of which were positive for syphilis. The

occurrence of Hutchinson's teeth at a proportionately higher rate in older children was interpreted as a quantitative reduction of congenital syphilis in recent years.

J. M. A. EIRE, DUBLIN

The control of streptomycin. J. W. Bigger, J. M. A. Eire, 25: 51-52, Oct. 1949.

Medical Research Council consents to resume control of the drug.

J. PATH. & BACT., EDINBURGH

James McIntosh. Obituary. J. Path. & Bact., 61: 285-299, Apr. 1949.

A description of his work in syphilology and a comprehensive bibliography are presented.

UNIV. SOUTH. CALIFORNIA M. BULL., LOS ANGELES

Aureomycin. A review. Edwin G. Troutman and Mary O. Flesher. Univ. South. California M. Bull., 1:12-16, July 1949.

A review of the literature on aureomycin, with particular reference to its pharmacologic properties and clinical applications. Aureomycin is the drug of choice in lymphogranuloma venereum and granuloma inguinale and is of value in penicillin-resistant strains of gonorrhea.

S T A T I S T I C S

Syphilis Infant Mortality Data, Centinental United States, 1933-48

Year	Number o	f deaths under	r 1 year of	Rate per 1,000 live births			
	White	Nonwhite	Total	White	Nonwhite	Total	
1933	794 757 768	845 856 740	1, 639 1, 613 1, 508	0. 44 . 41 . 41	2. 95 2. 84 2. 77	0. 79 . 74 . 70	
1936	768 707 654 563 513	808 815 790 737 738	1, 576 1, 522 1, 444 1, 300 1, 251	. 41 . 37 . 33 . 28 . 25	3. 07 2. 96 2. 81 2. 60 2. 52	. 73 . 69 . 63 . 57	
1941	395 363 305 287 256	647 482 434 459 428	1, 042 845 739 746 684	.18 .15 .12 .12	2. 03 1. 50 1. 28 1. 35 1. 26	. 41 . 30 . 25 . 27 . 25	
1946 1947 1948	193 168 151	345 349 287	538 517 438	. 07 . 05 . 05	.92 .82 .63	. 16 . 14 . 12	

Source: National Office of Vital Statistics: Vital Statistics of the United States, 1933–1947; unpublished data, 1948. FSA—PHS Division of Venereal Disease, Office of Statistics, 2–2–50 (MRB-JWM) mrb.

Summary of Reported Syphilis Mortality, Continental United States, 1933-48

	·	Non- white	39.3 42.1 40.8	43.4 45.1 44.0 31.9 30.2	25.9 21.2 20.7 18.3 16.4	14.3 12.9 11.4
Other forms		White	5.5 5.5 5.5 5.5	6.6 6.3 1.4 1.1	6.6.6.6.6.6.6.6.6.6.6.6.6.6.6.6.6.6.6.	1.22.2
	Ot	Non- white Total	9.3	9.01 9.09 9.09 9.08	6.7.7.4.4 2.8.8.0 2.0	23.5
	yph-	Non- white		5.1	4. బ. బ. బ. బ. బా & బ బా బ	2.5
tailed e	Congenital syphilis 2	White		. 5	<u> यं यं धं धं धं</u>	222
ı by de	Cong	Total		1.0	%r-999	4.4%
oulation	n 1	Non- Total	4.2 4.1	4.00.00.00 00.00.01.01	7.5 6.1 6.0	6.3
lod 000	Aneurysm	White	1.6 1.6 1.7	2.1.1.8 2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2	2.0 1.8 1.7 1.8 1.8	1.7 2.0 2.1
per 100,	An	Non- white Total	1.9	23.22.0 23.00 8	222236	22.2
h rate		Non- white	8.9.8	დ.დ.დ.დ. ც. 4 17 ი დ	9.1 10.5 11.5 11.3	9.5
Syphilis death rate per 100,000 population by detailed cause	Paresis	White	3.1 3.0 3.0	9999999 96888	999999 55554	1.8
	Loeomotor ataxia	Total	က် လုံ လုံ တေသ ဟ	00000000000000000000000000000000000000	0.00.00.00 0147070	2.9
		Non- white Total	0.0	∞ ⊕ \rac{1}{1} \disp \	ښښښښښ	446
		White	0.9	∞ ⊱စခဲ့		0,000
	Loeor	Non- white Total	0.9	87-99	24244	4.00.00
e to	m all	Non- white	3.72 3.83 3.78	3.70 4.15 4.08 3.93	3, 58 3, 41 3, 30 3, 19 3, 08	2.89
nt du	syptims of wear deaths from all eauses	White	1.06 1.06 1.04	1.04 1.05 1.08 1.01 1.01	. 92 . 86 . 81 . 76	. 59
		Total	1.41 1.44 1.40	1.40 1.43 1.49 1.41 1.34	1. 27 1. 18 1. 11 1. 06 1. 06	88.8
death	000,000	Non- white	52. 4 56. 6 54. 0	56.8 58.0 58.2 55.1 54.3	47. 5 42. 5 42. 1 39. 6 36. 9	32. 1 29. 9 26. 9
Ilis	rate (per 100,000 population)	Total White	10.9 11.3 11.0	11.5 11.4 11.1 10.4 9.9	98.88 9.66 9.77 9.00	6.6
Syphilis	rate		15.1 15.9 15.4	16.2 16.1 15.9 15.0	13.3 12.2 12.1 11.3	20.88
21:3	Silling	Non- white	6, 686 7, 274 7, 006	7, 422 7, 623 7, 717 7, 371 7, 305	6,600 5,975 5,898 5,501 5,170	4, 715 4, 504 4, 138
4	Number of syphius deaths	White	12, 298 12, 801 12, 554	13, 279 13, 179 12, 928 12, 233 11, 701	11, 128 10, 370 10, 365 9, 415 8, 892	8, 240 8, 167 7, 478
7		Total	18, 984 20, 075 19, 560	20, 701 20, 802 20, 645 19, 604 19, 006	17, 728 16, 345 16, 263 14, 916 14, 062	12, 955 12, 671 11, 616
	Year		1933 1934	1936 1937 1938 1939	1941 1942 1943 1944	1946 1947 1948

Aneurysm of the aorta designated as syphilitie beginning 1939. Prior to this date, aneurysm had little weight in the Manual of Joint Causes of Death and was frequently tabu-2 Congenital syphilis data were not tabulated separately prior to 1939 and are included in "Other forms" 1913-38. lated under associated eauses.

Source: Bureau of the Census: Vital Statistics Rates in the United States, 1933-40; Mortality Statistics, 1933-36; Vital Statistics of the United States, 1933-40; Mortality Statistics of the United States, 1933-47; 1948 unpublished data from the National Office of Vital Statistics: 1949 rate—Current Mortality Analysis, vol. 7, No. 9, 1-5-50.

FSA—PHS Division of Venereal Disease, Office of Statistics, 2-1-50 (MR-Bmrb).



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The JOURNAL of

VENEREAL DISEASE INFORMATION

Volume 31

May 1950

Number 5

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Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription Price: Domestic 75 cents a year; foreign \$1.15

Reports of the North Carolina Syphilis Studies 1

IV. Some Problems in the Evaluation of Venereal Disease Education

John J. Wright, M. D., M. P. H., Cecil G. Sheps, M. D., M. P. H., and Alice E. Gifford, M. N., C. P. H. N.

Introduction

A wide variety of activities labeled "education" are carried on as part of present-day venereal disease control programs. Some of these educational efforts are directed toward reducing promiscuity. Others attempt to bring about early recognition and reporting of venereal disease.

The number of pamphlets distributed, movies shown, and educational talks given indicates the amount of activity in this part of the program, just as the number of persons attending lectures and writing for free literature indicates the degree of interest or curiosity on the part of the public. However, this information does not necessarily provide a measure of the effectiveness of the program. And it is, after all, the effectiveness of the educational procedures which must be tested before such a program can be evaluated. Such evaluations can then provide a basis for planning effective, economical, and precise educational programs.

An examination of the literature on the role of education in venereal disease control reveals general agreement that objective evaluations are extremely difficult if not impossible to make. The published evaluations of educational projects fall into three groups:

- 1. Those based on the subjective impressions of the recipient of the education or of an observer (1, 2, 3).
- 2. Those attempting to measure objectively the amount of factual information possessed by the recipient (4, 5, 6).

3. Those attempting to detect and measure changes in behavior resulting from education (7, 8, 9, 10, 11, 12, 13, 14, 15, 16). These studies deal either with one particular educational medium or with an entire program utilizing several mediums and approaches.

A typical example of studies in the first group is that by Getzoff (1), who describes a questionnaire given to a group of enlisted men to determine their response to venereal disease education. These men were asked to indicate, among other things, the source and extent of their preinduction sex hygiene knowledge; their own reaction to the use of lectures, posters, pamphlets, films, and slides in venereal disease education; and the extent to which each of these mediums had modified their own sex behavior and increased their understanding of venereal disease. A test of factual knowledge was given to measure the level of information actually possessed by each man.

Carpenter, ct al. (4) describe a study of the second type of project evaluation. This was an experiment designed to measure the extent and accuracy of knowledge about venereal diseases possessed by grade school students and to evaluate several mediums and methods for teaching the control of these diseases. Objective tests were given before and after the teaching period so that gains in information could be accurately assessed. In this experiment a control group was used, and the results were tabulated according to the age of the student.

Studies in the third group which attempt to evaluate one or more of the behavior changes resulting from venereal disease education include that by Cowper and Clark (7) which deals with two

¹ From the School of Public Health, University of North Carolina. These studies are supported jointly by grants from the International Health Division of the Rockefeller Foundation and the North Carolina State Board of Health.

groups of elinic patients receiving routine therapy for syphilis. A earefully instructed group is compared with a easually instructed group in terms of clinic visits and delinquency during the treatment period. A number of ease-finding projects which feature educational campaigns in combination with mass examinations and blood tests have recently been described (9, 10, 11, 12, 13, 14, 15, 16). Results have been evaluated in terms of the increased number of venereal disease cases reporting during and after the campaign, usually using a previous comparable period as a control.

To what extent do such studies provide reliable measures of the effectiveness of various aspects of venereal disease edueational programs? The validity of an individual's self-appraisal of the relative contributions made to the sum total of his venereal disease knowledge by divers mediums and approaches may be seriously questioned because it invites a subjective report in an area where behavior is motivated by a highly complex web of forces and experiences. The motivations of human sex behavior require deeper study than the superficial questioning of an individual.

When objective tests are administered to a population, reliable information is usually obtained regarding the extent and accuracy of knowledge about venereal disease possessed by the persons tested. The usefulness of such data is increased if the data are tabulated on a race, sex, age, or other specific basis. When the effectiveness of a particular medium or approach is being tested, a control must always be used in the form of a pretest of knowledge or a control group of eomparable persons. In interpreting tests administered shortly after the learning experience, the loss of knowledge due to the passage of time must be eonsidered. The use of retention tests would help to overcome this difficulty.

The essence of the effectiveness of a venereal disease educational program is the extent to which it results in desired changes in overt behavior in relation to venereal disease control. For this rea-

son, studies are valuable which measure the volume of voluntary reporting which follows an educational program aimed at routine sereening or the investigation of suspicious lesions or symptoms. Such studies must use valid eontrols, such as a eomparable group, area, or period of time which differs from the experimental group only with respect to the educational program. The increased volume of reporting becomes more meaningful when it is analyzed in terms of race, sex, age, and stage of disease. Previous reports of the North Carolina Syphilis Studies (17, 18) have shown that there are important differences in the degree to which reliance can be placed on the patient's initiative in the discovery of venereal disease, depending upon specific factors such as those listed above.

In 1944, Anderson (19) stated that "Nowhere in the field of health education have adequate tests been developed to measure the relative effectiveness of various educational procedures or even to measure the accomplishments of the educational program as a whole. In venereal disease education this is particularly true." It appears that even though progress has been made since that time, there is still a great deal of eonfusion as to how the effectiveness of education can be measured.

The Construction of an Evaluation Device

Evaluation by objective methods, instead of by intuition, is an essential and integral part of any educational program. Basic patterns have been developed by research workers in education which, it is believed, ean be applied in the field of venereal disease education. Remmers and Gage (20) outline this procedure as follows:

- 1. Statement of the purpose and content of evaluation.
- 2. Construction or selection of an evaluating device.
- 3. Administration of the evaluating device.
 - 4. Interpretation of the data yielded by

the evaluating device (data related to the purpose and content of the evaluation).

5. Evaluation of the evaluating device in terms of the success with which it serves its purpose and the extent to which it can be improved.

Applying the foregoing principles, it is necessary first to define clearly the objectives of venereal disease education before an evaluation device can be selected or constructed. These may be stated as follows:

- 1. To impart information to the individual so that he will know what these diseases are, how they are spread, and how they can be avoided and, at the same time,
- 2. To motivate changes in individual behavior which will:
- (a) Alter sex habits, resulting in less promiscuity and/or
- (b) Result in the greater use of prophylaxis by individuals and/or
- (c) Bring infected individuals to treatment without delay.

The evaluating device or test must then be constructed so as to provide an accurate measure of the extent to which a particular objective has been accomplished. Gains in factual information are more easily measured than are those objectives associated with overt behavior changes. These two objectives are separate and distinct and cannot be measured by the same device. Thus the commonly used questionnaire which measures the extent to which a given individual has absorbed the facts cannot necessarily be interpreted as a measure of the extent to which he would use these facts. indeed small comfort to know that the syphilis patient with a lesion of 3 weeks' duration "knows all about venereal diseases." Larimore and Sternberg (8), on the basis of the Army experience, have said ". . . we found no significant difference between the knowledge about venereal disease possessed by groups who have acquired venereal disease and those free of infection . . ."

Measurement of behavior changes is at all times difficult. The complexity of the motivations affecting sex behavior makes objective measurement in this area even more difficult. Methods of measuring promiscuity directly are not available. The extent to which prophylaxis is used does not ordinarily lend itself to objective measurement. In the Army during World War II, however, data were available regarding the extent to which prophylactic materials were supplied and facilities were used. Larimore and Sternberg (8) suggested that this was the best single criterion of the success of the Army education program. Lowered incidence rates might be interpreted as being due to achievement of the objectives involving changing sex habits and the use of prophylaxis. So many other complex factors are involved, however, that it would be impossible to delineate the part played by education alone.

The third objective involving behavior change is that of motivating individuals with suspicious lesions to seek diagnosis and treatment without unnecessary delay. This seems to offer possibilities for objective analysis. These individuals represent failures so far as preventing venereal disease is concerned. Once infected, however, they have a potential contribution to make to the control program in that their prompt attention to symptoms will shorten their period of infectivity. Successful education in this regard, therefore, involves the recognition of suspicious lesions or symptoms and their prompt investigation and treatment.

During World War II, an intensive educational program was carried on by all the armed services. Many and divers methods were used to impart venereal disease information and to effect desired behavior changes. Among the clear objectives of this program was that of motivating the service man to seek treatment without delay. Therefore, it would appear that a study of the readiness with which veteran and nonveteran groups reported for treatment once suspicious lesions had appeared could be used as a means of measuring the extent to which this objective was achieved. The purpose of this communication is to report on a study of comparable groups of veterans and nonveterans, who reported voluntarily with symptoms of gonorrhea, in order to determine whether there were any significant differences in the readiness with which these groups reported for diagnosis and treatment.

Method of Study

The organization and field of operation of the North Carolina Syphilis Studies have been described in a previous communication (17). Although these studies have been devoted primarily to syphilis, careful records were available regarding certain aspects of the cases of gonorrhea which came to the attention of the health department. It was the policy to interview as many of the patients with gonorrhea as time permitted in order to obtain epidemiologic information, including veteran status and the duration of gonorrheal symptoms. The data presented here include all interviewed Negro male patients 19 years of age and older who, because of gonorrheal symptoms, reported voluntarily to the Durham City and County Health Department during the three calendar years 1946-48. The source of data used in this study was the epidemiologic record filled out by the trained interviewer at the time of each interview.

Veterans were defined as those who had served 3 months or more in a branch of the armed services. Since the number of veterans under the age of 19 years in the clinic population during this period was too small to use for comparison with the number of nonveterans, age 19 years was used as the lower limit of the group studied. The duration of symptoms in this study indicates the total number of days on which symptoms were present, the day of onset, and the day of clinic admission, each being counted as 1 day. The day of clinic admission in every case represents the initial attempt of the patient to secure medical care. Since this area is served by a full-time venereal disease clinic which is open every day, as well as two evenings each week, free medical care was readily available to all the patients. In all cases, the clinical diagnosis of

gonorrhea was confirmed by laboratory tests. Cases among white patients were not included because of insufficient numbers.

The data were classified and tabulated by age, veteran status, and duration of gonorrheal symptoms. The tables present the data which are discussed. It will be noted that in some instances the percentages do not add up to 100 percent. The differences in summation are due to rounding. The Chi-square goodness of fit was used to test the statistical significance of the data.

Results of Study

A total of 1,210 interviewed cases was available for study. Of this group, it was necessary to omit 125 cases (10.3 percent) because of incomplete information pertaining to either military service or duration of symptoms. Of the 1,085 cases analyzed, 615 (56.7 percent) were veterans, and 470 (43.3 percent) were nonveterans.

Distribution of Cases by Age Group and Veteran Status

Table 1 shows the age distribution of entire sample. Three-year the. groups were used because it was believed that small spans in the age group 19-30 years might reveal differences which would otherwise be obscured. The lower section of this table shows the age distribution of all Negro' male gonorrhea cases, age 19 years and over, diagnosed at the clinic in 1947, the middle year of the study. In view of the similarity of the two age distributions, it can be assumed that there was no bias in the selection of cases to be interviewed in favor of any one group.

Duration of Symptoms by Age Group and Veteran Status

Table 2 shows the cumulative percentages of veterans and nonveterans reporting for diagnosis not later than the second, fourth, and sixth day of duration of symptoms. These, with the addition of the cases which reported for diagnosis

Table 1.—Distribution of cases, by age group and veteran status

		Age group (years)									Total	
Cases studied ¹ (1946–48)	19-21		22-24		25-27		28-30		Over 30		Num-	Per-
	Num- ber	Pcr- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	ber	cent
VeteranNonveteran	173 171	28. 1 36. 4	234 77	38. 0 16. 4	118 78	19. 2 16. 6	45 63	7.3 13.4	45 81	7.3 17.2	615 470	100 100
TotalAll cases ² (1947)	344 200	31. 7 30. 7	311 188	28. 7 28. 8	196 113	18. 1 17. 3	108 60	10 9. 2	126 91	11. 6 14	1, 085 652	100 100

Negro males who reported to clinic voluntarily because of gonorrheal symptoms and who were interviewed.
 All Negro male cases of gonorrhea diagnosed in the same clinic in 1947.

Table 2.—Cumulative percentages showing duration of symptoms at time of diagnosis, by age group and veteran status

		Length of time											Tradal 2			
	2 days or less		4 days or less			6 days or less				Total 3						
Age (years)	Veteran Non-veteran		Ve	Veteran Non- veteran		Veteran		Non- veteran		Veteran		Non- veteran				
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
19-21 22-24 25-27 28-30 O ver 30	83 120 59 19 17	48 51.3 50.0 42.2 37.8	76 31 31 23 23	44. 4 40. 2 39. 7 36. 5 28. 4	144 192 98 34 34	83. 2 82. 0 83. 0 75. 6 75. 6	122 51 53 49 51	71. 3 66. 2 67. 9 77. 8 63	158 208 102 37 37	91. 3 88. 9 86. 4 82. 2 82. 2	140 59 58 53 58	81. 9 76. 6 74. 4 84. 1 71. 6	173 234 118 45 45	100 100 100 100 100	171 77 78 63 81	100 100 100 100 100

later than the sixth day, comprise the groups in the column headed "Total." That veterans in the age groups 19-27 years consistently reported for diagnosis sooner than did nonveterans is graphically represented in figure 1. Although this difference is not statistically significant at the second day, it is highly significant at the fourth and sixth days. In the age group 19-21 years, 83.2 percent of the veterans reported by the fourth day, as against 71.3 percent of the nonveterans; at the sixth day, 91.3 percent of the veterans had reported, as against 81.9 percent of the nonveterans. same trend is apparent in the 22- to 24year age group, wherein 82 percent of the veterans, compared with 66.2 percent of the nonveterans, reported by the fourth day, and 88.9 percent of the veterans, compared with 76.6 percent of the nonveterans, reported by the sixth day. The difference between the veteran and nonveteran groups is still apparent in the 25- to 27-year age group. By the fourth day, 83 percent of the veterans had reported, contrasted with 67.9 percent of the nonveterans; by the sixth day, 86.4 percent of the veterans had applied for examination, as contrasted with 74.4 percent of the nonveterans.

Data relating to patients over the age

Duration: time lapse in days between onset of symptoms and clinic admission.
 Negro males who reported to clinic voluntarily because of gonorrheal symptoms and who were interviewed.
 All cases studied, including patients whose symptoms had been present longer than 6 days.

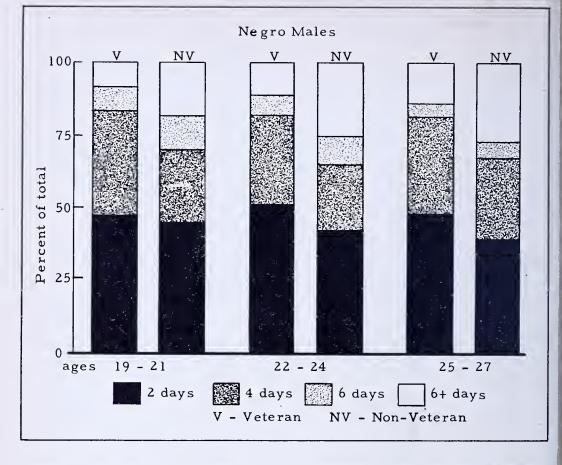


FIGURE 1.—Gonorrhea patients applying for clinic admission, by intervals following onset of symptoms, by age group, and by veteran status.

of 27 years did not demonstrate any clearly discernible trend and were not statistically significant.

Discussion

There can be little doubt as to the central role of education in venereal disease control—education directed at the general public, special population groups, patients, and their contacts. Although such an educational task is very complex, it must nevertheless be clearly purposeful. Because it is possible to outline distinctly the objectives of venereal disease education, a knowledge of its success or failure in any specific aspect should form the basis of the developing program in this field. Prolonged and sincere effort plus the expenditure of increasingly large sums of money on audiovisual materials

is hardly sufficient justification for continuing a program which has not been objectively evaluated.

Fundamental to the 'adequate evaluation of a program of education is a clear delineation of its objectives. The basic objectives of venereal disease education have been seen to involve two distinct, though possibly related, goals—the acquisition of facts and the modification of behavior. There is at present little convincing evidence that the second goal is automatically reached when the first has been achieved. There are few studies in the literature which measure behavior changes resulting from education with any degree of accuracy. The need for studies of this type is not lessened one whit by the complexities involved.

One desired behavior change which is

perhaps the least difficult to measure is that of the effect of education in motivating infected persons to report for diagnosis and treatment without delay. Using a series of 1,085 Negro males, an analysis has been made of the time lapse between the onset of symptoms and the first attempt to obtain medical care. Comparisons of the duration of symptoms in veterans and nonveterans were made on an age-specific basis. As has been mentioned, one of the clearly defined objectives of the venereal disease educational program of the armed services was to motivate the service man with suspicious symptoms to seek diagnosis and treatment without delay. For these reasons it was believed that an analysis of such data might indicate the degree to which this educational program had achieved the single objective outlined above. was found that veterans in the age groups 19-27 years with gonorrheal symptoms reported for diagnosis significantly sooner than did nonveterans of the same age. This difference was not evident among the patients 28 years of age and over.

Some discussion is warranted regarding the validity of our assumption that, for the purpose of this study, the veteran and nonveteran groups differed only with regard to the exposure of the veteran group to the educational program of the Clearly, both armed services. throughout their lives had been equally exposed to the various educational measures directed at the general public. be considered is the possibility that the basis of selection for military service may have created a bias in favor of inducting persons with a greater receptivity and learning capacity than those who were rejected. In that event, differences in the readiness with which veterans and nonveterans reported for diagnosis might be ascribed to differences between these groups in receptivity to the general public educational program and not to the effect of the program to which only the veteran group had been exposed.

Among the criteria used for selective service rejection or deferment were such important items as physical defects covering a wide range of disabilities, illiter-

acy, intelligence deficiency, dependency, and essential agricultural or industrial activity. Of these, intelligence deficiency and illiteracy might well be expected to lower the receptivity of the nonveteran group to general public venereal disease education. As the war progressed, however, illiteracy per se no longer was used as the sole basis for rejection. In North Carolina the proportion of Negro registrants rejected for either of these two reasons is estimated at being a little less than 7 percent during the entire war period (21). It appears justifiable to assume that the I. Q. of the registrants rejected for other reasons probably followed a normal distribution. It is therefore difficult to gage the extent to which the basis of selection for military service may have created a bias in favor of inducting those persons who had a greater receptivity and learning capacity than those who were rejected. If it had been possible to administer objective psychological tests to both veteran and nonveteran patients at the time of clinic admission, our information on this point would be more complete and more reliable.

This analysis does not take into account the length of service aside from the fact that all patients classified as veterans served at least 3 months. The venereal disease control program in the services was designed so that each inductee was exposed to a rather intensive educational program at the beginning and at the end of his service. Although this education was continued throughout the period of service, the difference in emphasis in the various services and in the various geographic areas seriously limits the value of taking length of service into account in this study.

Our data suggest that the venereal disease educational program of the armed services was effective insofar as achieving the objective of motivating veterans with symptoms suggestive of gonorrhea subsequent to their period of service, to seek diagnosis and treatment with a minimum of delay. This effect was demonstrated only in the younger age groups. This might be due to the relatively small numbers of cases in our series in the age

group 28 years and over. It might also be postulated, however, that behavior patterns in this field become more fixed with increasing age.

It must be pointed out that, to the extent that the above findings are valid, they are valid only with regard to gonorrhea and do not necessarily apply to syphilis. There has been an awareness among clinicians, largely unexpressed, that a urethral discharge is more likely to cause a man to seek medical attention than is the presence of a genital sore. Evidence supporting the validity of this concept is found in previous reports of the North Carolina Syphilis Studies. In a series of 229 Negro males with primary lesions, it was found that only 63.3 percent came to diagnosis on their own initiative (17). This is to be compared with the fact that in a series of 1,289 Negro males with gonorrhea, 91.3 percent came to diagnosis on their own initiative (18).

Summary

Scientific, efficient, and economic educational programs in venereal disease control must be based upon the objective assessment of the success or failure of such programs. Although such evaluation presents many complex difficulties, the component parts of this problem can be separated. Commonly used approaches to the evaluation of programs in this field are discussed and analyzed. Attention is paid to the problems involved in the construction or selection of an evaluation device for venereal disease education.

One of the objectives of the venereal disease educational program of the armed services was that of motivating the serviceman to seek diagnosis and treatment without delay. Comparison of the time lapse between the onset of symptoms and the date of application for clinic care of a group of veterans and nonveterans with symptoms of gonorrhea was used as the device to evaluate the extent to which this objective was achieved. These data, based on a study of 1,085 cases, indicate that the educational program of the armed services was effective in motivating younger Negro veterans with gonorrheal symptoms to report for medical

care sooner than nonveterans of the same age with the same symptoms.

Acknowledgment

The authors wish to express appreciation to J. H. Epperson, Superintendent of the Durham City and County Health Department, Dr. O. L. Ader, Director of its Venereal Disease Clinic, and the clinic staff whose cooperation made this study possible.

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The False-Positive Reaction in Serology of Syphilis: The Presence of an Antiacetone Soluble Substance in Human Serum¹

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The purpose of this paper is to demonstrate (1) the existence in some human serums of a substance, possibly an antibody, which reacts with impurities in syphilis antigen; and (2) the relationship (but not identity) of this antibody to the syphilis reagin. These impurities, moreover, can be used in certain instances to demonstrate the existence of a false-positive reaction in the serology of syphilis.

In discussing the possible causes for false-positive serologic reactions for syphilis, Davis (1) reasoned that these may be caused by the presence in serum of (1) an antibody or "reagin" identical with that produced in response to syphilitic infection; or (2) an antibody differ-

ing in some ways from this antibody but cross-reacting with the antigen, or some fraction of the antigen, which is used in serologic tests for syphilis. Davis felt that if hope exists for solution of the false reaction, it rests on the assumption that false-positive serums fall into the second category, that of the cross-reacting but not identical antibodies. He felt that both types of antibodies might be differentiated, ultimately, by chemical or immunologic means.

In 1937, Mackie and Anderson (2) observed that an acetone-soluble fraction of sheep heart, usually discarded in the preparation of antigen used in serologic tests for syphilis, flocculated with both non-syphilitic and syphilitic human serums.

¹ From the Bureau of Laboratories, New York City Department of Health.

These investigators demonstrated the difference between the acetone-soluble fraction and the acetone-insoluble fraction, i. e., the usual syphilis antigen, by absorption experiments using seropositive rabbit serums.

It is possible, as we shall demonstrate, that certain false-positive human serums contain large amounts of an antibody which reacts with the impurities in the syphilis antigen.

Method

A. 1. The preparation of one acetonesoluble antigen (to be called AS I antigen in this paper) was accomplished by extracting 30 gm. of beef heart powder with 100 ml. of acetone for 5 days, with brief shaking each day, followed by filtration through fat-free filter paper. After the solution was centrifuged and the precipitate discarded, the acetone was evaporated at room temperature and the residue redissolved in 95-pcrcent ethyl al-The alcoholic solution was then added to 1-percent cholesterinized alcohol, and an antigen was prepared following the procedure for the Mazzini slide test (3). The technic of the Mazzini slide test was used with this AS I antigen.

2. Another antigen (AS II) was prepared from alcoholic uncholesterinized Mazzini antigen extract as follows: 50.0 ml. of the extract was evaporated to dryness. To the residue was added 100 ml. of acetone, shaking occasionally. The next day the solution was filtered, the acetone evaporated, and the residue redissolved in fresh acetone and filtered. This process was repeated four times. After final evaporation of the acetone, the residue was dissolved in 95-percent ethyl alcohol, cholesterinized, and an antigen was prepared as stated above for AS I.

B. The agglutinin-absorption experiments were performed by preparing double-strength emulsions with the AS antigens and with the antigen for the VDRL slide test (4): 0.8 ml. of each AS antigen was added to 3.0 ml. of Mazzini buffered saline solution; 1.0 ml. (instead of the customary 0.5 ml.) of VDRL slide

test antigen was added to VDRL buffered saline solution; and 1.0 ml. of serum was added to 1.0 ml. of antigen emulsion (either the AS or the VDRL). The mixture was agitated in a Kahn shaker for 5 minutes, followed by 25 minutes in a 37° C. water bath, and finally by 10 minutes in an angle centrifuge. The supernatant was then tested for antibodies against the AS and/or the VDRL antigens.

Results

The existence of an antibody which reacts with the AS antigen was demonstrated in 109 (2.1 percent) of 5,048 specimens which were submitted for routine serologic examination. About 16 percent of these specimens were reactors when tested by the Mazzini slide test. Of 2,016 Mazzini "negative" specimens, 0.5 percent reacted with the AS antigens.

Since the VDRL slide test uses a purified antigen consisting of a cardiolipin-lecithin mixture, and the Mazzini slide test, in our hands, is used as a "screen" test, we examined the group of serums that might be expected to yield a large number of false-positive reactions, i. e., the Mazzini-reacting, VDRL-nonreacting specimens. We found that 74 (10 percent) of 725 serums in this group were AS reactors.

The large number (10.2 percent) of AS reactors in the latter group, compared with 0.5 percent in the serums failing to react with the Mazzini antigen, suggested the possibility that one of the reasons for the false-positive reactions so often concountered in the Mazzini "positive," VDRL "negative" group of serums may be the presence of an antibody in these serums which reacts with an AS material present in the Mazzini antigen. We therefore attempted to obtain an AS antigen from the Mazzini antigen extract.

In table 1 it is noted that an AS antigen II can be produced from the uncholesterinized Mazzini antigen extract and that this AS antigen is similar to the AS material extracted from the beef heart. Moreover, the absorption experiments (table 1) indicate that the AS material and the cardiolipin-lecithin an-

Table 1.—Differentiation of cardiolipin-lecithin antigen (VDRL) from acetonesoluble antigen (from beef heart (I) and from Mazzini antigen (II)) using pooled human serums

Pooled	A branched bas	Tooted be	Serum dilution									
serum	Absorbed by—	Tested by—	1	2	5	10	20	40	80	160		
A	Unabsorbed	VDRL AS I AS II	4 4 4	4 4 4	4 4 4	4 4 4	± 3 2	=	=	=		
	VDRL	VDRL AS I. AS II.	_ _ _	=	_	=	=	=	=	- -		
	AS I (beef heart)	VDRLAS IAS II	4 - 1	3	Ξ	=	=	=	=	=		
	AS II (Mazzini antigen)	VDRLAS IAS II	$\frac{4}{1}$	- -	=	=	_	Ξ	_ _ _	- - -		
В	Unabsorbed	VDRL	- 4		4	±	=		<u>i</u>	3		
-	VDRL	VDRLAS I	- 4	4	_	=	=	=	-	- 3		
	AS I	VDRL AS I	=	Ξ	-	=	-	_	1	3		

tigen, while related, are not identical antigens. There is, therefore, some basis for assuming that the AS material in the Mazzini antigen is responsible for some of the false-positive reactions in serums containing an antibody against the AS antigen.

The data already presented indicate that AS antigens will react with an antibody in certain serums, even though the serums do not react with the cardiolipin-lecithin antigen. In table 2 we note that a serum reacting to a high titer with the VDRL antigen in many instances also reacted with the AS antigen. This, of

course, would be expected with crossreacting antigens and antibodies.

In view of the results obtained, it was felt that the AS antigen could be utilized in some instances as a possible means of recognizing a false-positive serologic reaction. We therefore tested a number of serums of patients in whom the syphilologists in our clinic were particularly interested because of their clinical histories. The diagnosis of "syphilis" or "nonsyphilis" was made by the clinicians with no information from the laboratory as to the result of tests for substances which reacted with the AS antigen. Rep-

Table 2.—Reactivity of 220 human serums with AS antigen as compared with the VDRL slide test

	,				A	AS antige	n titers			·	
Number of specimens	VDRL titer	Nega- tive	Positive 1:1	Posi- tive 1:2	Posi- tive 1:5	Positive 1:10	Positive 1:20	Positive 1:40	Positive 1:80	Positive 1:160	Total
84	1:2 1:5 1:10 1:20 1:40 1:80 1:160	80 26 44 8 0 1	1 0 14 1 1 1 0	3 0 9 10 3 1	$egin{pmatrix} 0 \\ 0 \\ 1 \\ 2 \\ 4 \\ 0 \\ 0 \\ \end{bmatrix}$	0 0 0 1 0 0	0 0 0 0 0 0	0 0 0 0 0 0	0 0 1 3 1 1 0	0 0 0 1 0 1 0	$\begin{array}{c} 84 \\ 26 \\ 69 \\ 26 \\ 9 \\ 5 \\ 1 \end{array}$

Table 3.—Correlation of clinical opinion and laboratory findings on patients tested for AS antibodies

				Laboratory findings		
Patient	Date	Maz- zini	Kolmer	VDRL titer	AS titer	Clinical opinion
L. L	May 19 June 1 June 7 June 21 June 30 July 14 July 28 Nov. 26 Dec. 30	4 4 4 3 4 3 3 3 2 2	4 3 2 4 ± 3 - 4 1	Weakly positive () Weakly positive () () () () ()	Positive 1:2	Not syphilis.
P. P	May 20 May 27 June 5 June 11	3 3 3 2	4 4 ± 4	Positive 1:2	Positive 1:160 Positive 1:20 Positive 1:10	Not syphilis: pregnancy, normal child born.
M. M. M. J. L. W. S. R.	June 12 June 25 July 10 Sept. 22	1 3 2 1 4 4 4	2 - 2 4 4 4	Weakly positive (-) Positive 1:20 Positive	Positive 1:2	Not syphilis. Not syphilis. Not syphilis. Syphilis.
R. B		4 4 3 1 4 4	4 4 4 4 4 A C	Positive 1:10	Positive 1:2	Syphilis.

resentative results of this study are summarized in table 3. These results indicate some correlation between a diagnosis of syphilis by the clinician and greater reactivity of the serum with the cardiolipinlecithin antigen (the VDRL slide test) than with the AS antigen. On the other hand, no diagnosis of syphilis could be made by the clinician in those cases (admittedly few in number) wherein the serum reactivity was greater with the AS antigen than with the VDRL antigen. Further work on the use of the AS antigen as a means of differentiating between true and false serologic tests for syphilis is necessary before this antigen can be used routinely by serology laboratories.

Discussion

It must be emphasized that it is not suggested that all false-positive reactions are caused by the presence of AS-reacting substances in the serum. However, some false-positive reactions, as has been demonstrated, are undoubtedly due to the

presence in the serum of a substance which either will react with acetone-soluble material present in antigens used in serologic tests for syphilis or will cross-react with the purified cardiolipin-lecithin antigens.

The AS antigen is by no means a pure antigen, but probably consists of at least two different antigenic substances soluble in acetone. This thought is presented because of the bizonal activity of the AS antigen as observed by us (table 1, serum B) as well as by Mackie and Anderson (2). In all probability, several nonsyphilis antigens similar to the AS antigen described in this paper can be isolated from beef heart which would help in recognizing a false-positive serologic reaction.

Summary

1. Evidence is presented to indicate the presence in certain human serums of a substance which reacts with the acetone-soluble (AS) material usually discarded

in the preparation of syphilis antigens.

- 2. The AS and the cardiolipin-lecithin antigens are not identical, but will cross-react with each other.
- 3. The presence of the AS material in the Mazzini antigen may be responsible for some of the false-positive reactions encountered.
- 4. The use of the AS antigen in conjunction with the VDRL slide test is suggested as a means of recognizing some of the biologic false-positive reactions; until further work is done, however, it is not offered as a new verification test for syphilis.

References

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Education and Mass Blood Testing an Effective Syphilis Case-Finding Combination¹

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Finding existing cases of syphilis in a given population is a fundamental part of the control program. Today's cases are links in biologic and pathologic chain reactions in the population that project themselves into the immediate and distant future to form the problem of 5, 10, and 20 years hence. There is a great test tube containing the American population and the spirochete. The spirochete is reacting upon the human content of this test tube to precipitate and inactivate the population by crippling and death. syphilis control workers, we pour into this tube certain ingredients in the form of case finding, education, and treatment that reverse the biologic reaction, causing precipitation and inactivation of the spirochete, preventing it from destroying the human content of this test tube. The proportion and the total amount of each of these ingredients added to this test tube through the control program will determine the total precipitate of human wreckage. The spirochete can be almost eliminated, and it is our business to do so.

Those responsible for syphilis control are obligated to use methods that will discover the greatest number of cases possible with the least amount of money and effort and that will cause the most rapid decline in the incidence and prevalence of this disease. The principal methods of case finding are contact investigation, blood testing of whole or special groups such as hospital admissions and those under general medical care, and examination of lesion suspects brought to diagnosis through education.

Presented at the Venereal Disease Control Seminar, Savannah, Ga., September 28-29, 1949.

Most States have used contact tracing as their primary method, and some continue to use it almost exclusively. Mississippi used it from 1938 until 1947 as the primary approach, and during this period it was the most useful method of discovering infectious syphilis. In 1947 and 1948 it became evident that, while contact tracing is useful, it leaves something to be desired in the total job of control in high incidence areas. It is expensive, reaches too small a percentage of the infected population, and is relatively slow. Being an epidemiologist by training and experience, I was slow to realize that syphilis control was lagging because we placed too much emphasis on finding certain individuals in the population rather than on doing something with the population that would cause many of those we were searching for to seek for themselves the control agency or physician.

The total number of cases of syphilis reported by clinics and public institutions in Mississippi reached 11,055 in 1947, and the number per year reported with primary and secondary syphilis reached the peak of 3,909 cases in 1946 (table 1). In 1948 and 1949 there was a decline in the number of cases reported, in spite of the fact that there was little or no decline in case-finding effort. In 1947, we decided to try the mass approach on a countywide basis in a high-prevalence county in order to determine its feasibility. The results were encouraging enough in the county chosen (Leflore) to cause us to continue the mass blood-testing approach county by county until the present time. with additions and refinements to the program being made as we went.

From special studies, we learned that it is necessary to present facts about syphilis rather than merely to ask the public to get a blood test because it is free or compulsory. Mere participation in a blood-testing program was possibly making some persons complacent (5 percent of the persons with primary or secondary syphilis found through contact investigation said they had not come to diagnosis of their own accord because they had had a negative result in a pre-

vious blood test). Too, it was found that mere mass testing had but momentary effect; without real education there was little carry-over and not as broad a coverage of the population. It was found necessary to educate those currently infected, those likely to become infected, and the community leaders whose enlightened support is needed in an effective control program. Hence, an educational program, as well as a mass testing appeal, was directed to all segments of the popu-The intensity of this education has been increased with each succeeding county.

What are the immediate results of conducting a mass blood survey and an educational program in a high-prevalence area? Facts are given in table 2 for four of the most recent counties surveyed.

The number of cases of primary and secondary syphilis discovered during the blood-testing period and within the first 2 or 3 weeks following the periods of testing ranged from three to five times the average monthly discovery rate prior to the survey. One of the significant results was the finding of an unusually large number of cases of congenital syphilis in children over 10 years of age.

Immediate results in two sample counties are shown in tables 3 and 4, which list the discovery of syphilis by classes and of gonorrhea for 3 months prior to the survey, 5 weeks during the survey, and 3 months after the survey.

It is evident from these two tables that the survey was an efficient method of locating primary and secondary cases of syphilis; even more important was the epidemiologic information derived from these cases, for this led to the discovery of even larger numbers of cases of primary and secondary syphilis in the 3 months following the survey than had been discovered during the survey. These tables also show that the majority of the cases found in the survey were early latent and late latent syphilis. Of considerable significance is the number of cases of neurosyphilis and congenital syphilis found during and immediately after the survey compared to the 3 months prior to the survey.

Table 1.—Number of cases of syphilis reported by Mississippi State Health Department facilities

Year	All stages	Primary and secondary	Congenital	Year	All stages	Primary and secondary	Congenital
1943	14, 012 8, 550 10, 158 9, 922	1, 432 1, 383 2, 641 3, 909	716 660 513 574	1947 1948 1949	11, 055 10, 191 10, 739	3, 876 2, 357 1, 328	728 779 1, 019

Table 2.—Results of mass blood survey in 4 counties in 1949

County	Number of blood tests	Number of patients brought to treatment with syphilis
Bolivar (July 20-August 25)	17, 347	1 1, 484
Sunflower (January 17-February 19)	11, 720	1, 050
Lowndes (May 23-June 11)	10, 466	975
Washington (March 21-April 23)	14, 660	1, 765

¹ Incomplete—116 suspects still pending.

Table 3.—Number of cases of venereal disease discovered in Sunflower County before, during, and after mass blood-testing and educational case-finding campaign

	3 months before survey		During surv		3 months after survey	
	Total cases	New cases	Total cases	New cases	Total cases	New cases
Diagnostic observations completed	(205)		(12, 988)		(999)	
Syphilis: Primary and secondary Early and late latent Neurosyphilis Congenital	15 16 5	15 5 3 1	35 703 130 81	33 551 90 66	44 249 62 24	42 209 45 18
Gonorrhea and other venereal diseases	48	45	52	52	66	61

Table 4.—Number of cases of venereal disease discovered in Washington County before, during, and after mass blood-testing and educational case-finding campaign

	3 months before survey		During sur		3 months after survey	
	Total cases	New cases	Total cases	New cases	Total cases	New cases
Diagnostic observations completed	(222)		(12, 238)		(2, 856)	
Syphilis: Primary and secondary Early and late latent Neurosyphilis Congenital	24 51 10 5	$\begin{bmatrix} 22 \\ 29 \\ 6 \\ 2 \end{bmatrix}$	47 589 116 54	$\begin{array}{c} 42 \\ 540 \\ 80 \\ 46 \end{array}$	51 834 152 70	46 666 102 63
Gonorrhea and other venereal diseases	43	42	10	10	90	89

Faced with the problem of the rapidly declining discovery of cases of primary and secondary syphilis all over the country, everyone desires tools that will increase the discovery rate of infectious syphilis or at least decrease the rate of decline of discovery. Evidence is accumulating in Mississippi that the mass blood survey, used in conjunction with an intensive educational program, not only has a marked temporary effect in finding cases, both early and late, but that it also produces results many months after the survey is completed, as shown by the number of primary and secondary cases found in a given county. An example of this is what happened in Leflore County, which was surveyed in the period February through June 1947. There were, on the average, about 10 cases of primary and secondary syphilis per month for 12 months before the survey, about 23 per month during the 5 months of the survey, and about 17 per month during the 12 months after the survey—an increase of 68 percent after the survey. A similar effect has been demonstrated in several other counties surveyed. On the basis of these facts it is evident that the mass blood survey, supported by a good area-wide educational program, is an efficient method of discovering primary and secondary syphilis in high-prevalence areas.

Educational Program

Since 1947, when we began using the survey approach, we have gradually strengthened the educational program for the public preceding and during the survey, and since January 1, 1949, great emphasis has been placed on this phase of the program.

With increasing emphasis on the educational program, there has been a considerable increase in the proportion of the population having blood tests, in the number of cases found, and in the general concern among the population about the problem. In Bolivar County, the educational program consisted primarily of night meetings for the public, radio and

press informational services, discussions with civic groups, and visits to private physicians.

Forty-five night meetings were so distributed over the county that they were within four or five miles of every citizen. They were held almost entirely in Negro churches and schools. The meetings centered around the showing of the film "Feeling All Right," which in all instances was well received, followed by a lecture illustrated with colored slides showing various phases of syphilis. portunity was given for questions and answers. These meetings were scheduled so that they would fall within the community where the blood testing would follow 2 or 3 days later. Prior to and along with this public-gathering type of meeting, every club that could be reached, such as civic and women's clubs, had a discussion meeting on syphilis. paper publicity was continuous. ever suitable radio stations were available, programs of different types were broadcast.

A new feature for promoting the program is sound equipment and a turntable mounted on an automobile. Preceding each informational meeting and each blood-testing clinic for 1 or 2 hours, this equipment was used effectively in a radius of 2 to 3 miles to announce the time and place of the meeting and to urge attendance. This equipment is such that it is audible for 1 or 2 miles, and it seemed to have considerable effect on attendance. Before beginning blood testing, letters were sent to all landowners, industrial leaders, preachers, teachers, and midwives, calling their attention to the program, the need for it, and the extent to which they could be of help. Several schedules of the blood-testing clinics and night meetings were sent with the letter. While the educational program was directed to all segments of the population through every conceivable channel, blood-testing stations were scheduled primarily for the convenience of the Negro population, in which the prevalence is so high.

Another phase of the educational program, added in the last three counties surveyed, consisted of visits to every physician in each county during the week prior to the beginning of the survey by a professional liaison officer of the Division of Preventable Disease Control, who had previously visited all the physicians of the State with reference to all public health problems. Upon this particular visit, physicians were informed of the purpose, plan, and procedure of the survey and how each physician could assist They were requested to take a blood specimen from any individual who asked for it, and each physician was supplied with from one to four dozen Keidel tubes for this purpose. In addition, they were informed that they would probably discover several cases in patients who would want private treatment and that there was no objection to private treatment provided an acceptable schedule was used. The result of this additional effort has been well worth while. Most of the physicians commended rather than criticized the program and worked closely with the health department in disposing of the cases. The professional liaison officer left with the physician a new schedule of treatment and some of the essential facts about diagnosis of syphilis now being used by the rapid treatment centers; in most instances this material was well received.

No syphilis control program is adequate without efficient continuous contact tracing, regardless of prevalence, population composition, or geography. This will continue to be so. As the prevalence of the disease declines in an area or segment of the population, it is probable that the job of case finding should veer more and more toward this approach as the sole method.

I am not a proponent of a mass blood survey in the entire population. Even in high-prevalence areas or population segments, it is useful only to the extent that it is accompanied by an intensive and extensive educational program. For effective control, we need to do more than ask the public to get a blood test because it is free or compulsory.

Conclusion

Experience with the combination of education and mass blood testing in Mississippi has convinced us of the following:

- 1. This is an efficient method of finding infectious cases of syphilis in high-prevalence areas and is a splendid adjunct to routine contact tracing.
- 2. Through this method, many latent cases of syphilis are discovered that would probably not be treated otherwise.
- 3. Thus far, the combined method has proved to be unexpectedly productive in discovering cases of congenital syphilis, even in areas in which an extensive prenatal supervision program has been carried on for many years.
- 4. The combined method serves to alert local health departments to the fact that there are still many cases of syphilis, in spite of marked decrease in incidence. There is a tendency for local as well as State-level staff to routinize their program and thinking and to develop a passive attitude based on accomplishment. For instance, more than one health officer has expressed doubt that enough syphilis remained in his area to make a survey sufficiently productive to justify this effort. One such health officer anticipated that only three or four thousand blood specimens would be taken in the survey; about eleven thousand were taken, however, and about fifteen hundred patients were referred to the rapid treatment center.
- 5. The mass survey provides an excellent approach, reason, and opportunity to conduct an educational program for all segments of the population. This is extremely important for the population segments who have or are likely to have syphilis and for those of the population who assume moral, economic, social, and educational leadership in the area. It is this sustained effort that will make the control program effective.
- 6. The mass survey calls to the attention of the greater part of the population within a short period of time not only that there is a syphilis problem but also that there is an active local health department trying to do something about this

and other problems. But for this, many people would know of the department only as an appendage of local government and of doubtful value.

7. It is believed that in certain areas and selected segments of the population the cost per case found through the survey is far below the cost of any other method of case finding.

8. Our experience with the combination of education and mass blood-testing approach has been so favorable that we are making one survey team a permanent part of our program. If funds could be found for a second team and if treatment facilities were adequate to take care of the increased load, a second survey team would be added to our program in Mississippi.

CURRENT NOTES AND REPORTS

VD Research Lab Moved to Atlanta

The Venereal Disease Research Laboratory, which was at the Marine Hospital in Staten Island, N. Y., for many years, is now located in the Communicable Disease Center at Atlanta, Ga. The move was made to carry out plans of the Public Health Service for coordination of serologic evaluation and applied research

activities in allied fields which are now being conducted at the Center.

The Laboratory, which remains under the technical supervision of the Division of Venereal Disease, will furnish the same research services to the State health departments that it offered in the past. Mr. Ad Harris, Chief Serologist, is Acting Director of the Laboratory.

Press and Radio Publicize 1949 VD Projects

In 1949, syphilis case-finding projects produced at least 1,300 news and feature stories from 695 newspapers in 567 communities. Four hundred and twenty radio stations in 375 communities carried 5,084 spot announcements and 1,936 programs.

Limited to the facts available to us, any accurate evaluation of coverage in terms of individuals receiving a direct message is impossible. The figures indicate, however, not only a good coverage, but a willingness of newspapers and radio stations to cooperate with local health campaigns.

Take Care of Yourself

A new pamphlet under the above title has just been issued by the Bureau of Venereal Disease Control, New York State Health Department. It is designed for use as a cooperative project between physicians, their syphilis patients, and the Health Department. The pamphlet will be included with each vial of penicillin requested by physicians from laboratories and laboratory supply stations throughout the State. Accompanying each booklet is an easily detachable slip addressed to the physician, asking him to pass the publication on to his patient.

The booklet is attractively designed and contains pertinent information intended to enable the patient to better understand his disease and the treatment which he is receiving.

At the back of the pamphlet is a short form which may be filled out by patients with early syphilis, and forwarded to the State Bureau of Venereal Disease Control. The information it contains will be treated as confidential and will be utilized in bringing under treatment, where necessary, the contacts of the patient.

The text of the pamphlet includes a definition of the disease, its first signs, its constant danger, pregnancy and syphilis, and, in conclusion, five important "things to remember."

The State Department of Health "Bulletin" reports that individual requests for the pamphlet may be addressed to the Office of Public Health Education, New York State Department of Health, 18 Dove Street, Albany, N. Y.

CURRENT LITERATURE

ACTA MED. SCANDINAV., STOCKHOLM

Gastroduodenal ulcers as a result of lesion or disease of the nervous system. Elio Tartarini. Acta med. Scandinav., 134: 346-370, Fasc. V., 1949.

In this review of the literature the author points out that gastroduodenal hemorrhages have been observed in patients suffering from tabes dorsalis.

AM. J. PUB. HEALTH, NEW YORK

Psychosomatic approach to venereal disease control. Chronic gonorrhea repeaters. Herman N. Bundesen, Frederick Plotke, and Henry Eisenberg. Am. J. Pub. Health, 39: 1535–1540, Dec. 1949.

Handling of individuals reinfected repeatedly with gonorrhea and factors which contribute to reinfection are discussed. A study of gonorrhea repeaters admitted to the municipal Social Hygiene Clinic, Chicago, showed they had a below-average intelligence quotient. A psychosomatic approach is recommended to achieve a more complete prevention program.

BRIT. J. VEN. DIS., LONDON

Venereal disease as a cause of infertility and sterility: Assessment and treatment. Reynold H. Boyd. Brit. J. Ven. Dis., 25: 179-184, Dec. 1949.

The role of syphilis, gonorrhea, chronic prostatitis, blockage of ejaculatory ducts, vesiculitis, vasitis, epididymitis, epididymo-orchitis, chronic cervicitis, salpingitis, and trichomonas vaginitis, in producing sterility in males and females is discussed. Several methods of treatment are suggested.

Reiter's disease. A. H. Harkness. Brit. J. Ven. Dis., 25: 185-201, Dec. 1949.

A discussion of several factors which the author believes establish the venereal origin of Reiter's disease. He describes the disease as an abacterial urethritis of venereal origin with bloodborne complications.

A mechanical pipette. Balbir Singh. Brit. J. Ven. Dis., 25: 202-204, Dec. 1949.

A mechanical pipette, easily prepared with materials salvaged from a small workshop, is described. Treatment of bismuth stomatitis with BAL (British anti-lewisite). Brit. M. J., No. 4638: 1213, Nov. 26, 1949.

Case of bismuth stomatitis, treated with BAL, is reported. Clinical response occurred immediately and improvement was continuous and rapid. Toxic symptoms were comparatively mild.

The use of procaine penicillin with aluminum monostearate in adults. E. J. Wayne, J. Colquhoun, and Joyee Burke. Brit. M. J., No. 4640: 1319-1322, Dec. 10, 1949.

Bacteriostatic levels were maintained for 24 hours in 42 of 43 individuals given 300,000 or 600,000 units of procaine penicillin in arachis oil with 2 percent aluminum monostearate,

The fate of the foreskin. A study of eireumeision. Douglas Gairdner. Brit. M. J., No. 4642: 1433-1437, Dec. 24, 1949.

The author contends that universal circumcision is not warranted as a prophylaxis against venereal disease.

BULL. VANCOUVER M. A., VANCOUVER

The treatment of aortic ancurysm. Bruce Shallard. Bull. Vancouver M. A., 26: 70-73, Dec. 1949.

Iodides have no place in treatment of syphilitic aortitis or aneurysm. Necessity for preliminary bismuth in use of penicillin is questioned. Cellophane treatment in selected cases appears to offer increased longevity. Illustrative case history is reported of patient treated by this method.

CALIFORNIA MED., SAN FRANCISCO

A multiphasie sereening survey in San Jose. C. Kelly Canelo, Dwight M. Bissell, Herbert Abrams, and Lester Breslow. California Med., 71: 409-413, Dec. 1949.

The survey, conducted on 945 employees in industrial establishments of San Jose, uncovered 13 cases of significant disease previously unknown to patients and 16 cases previously known. In several instances, where presence of disease was known, treatment was begun or resumed.

CARIBBEAN M. J., TRINIDAD

Acute gonorrhea in the male-analysis of

500 eases, M. A. Fawkes. Caribbean M. J., 11: 64-69, 1949.

Treatment consisted of 150,000 units crystalline penicillin G administered January to June 1947 at the Caribbean Medical Centre, Port-of-Spain. Cure rate was between 92.7 and 97.1 percent after an analysis of 383 of the cases.

DELAWARE STATE M. J., FARNHURST

Report of the committee on social hygiene. A. D. King, Chairman. Transactions: House of Delegates October 10, 1949. Delaware State M. J., 21: 272, Dec. 1949.

There are indications of definite progress in the control of syphilis and gonorrhea. Penicillin has decreased the incidence of [new] infection bringing about a reduction in the over-all case load of the treatment center.

DIS. NERV. SYSTEM, CHICAGO

Penicillin or malaria therapy in the treatment of general paralysis? (A clinico-anatomie study.) Walter L. Breutseh. Dis. Nerv. System, 10: 368-371, Dec. 1949.

A study-at the Central State Hospital, Indianapolis, included the comparison of a group of general paralytic patients treated with 10,000,000 units penicillin (50,000 units intramuscularly every 3 hours) with a group of similar patients treated with malaria alone. Since 10,000,000 units revealed the presence of spirochetes in the brain at autopsy, 15,000,000 units are recommended for safety reasons. The impression was that penicillin at least equals, if not excels, malaria therapy when administered in sufficient amounts.

Illinois M. J., Chicago

Studies on a new pyrogen fever treatment. Werner Lonsen and Erieh Liebert. Illinois M. J., 96: 186-190, Sept. 1949.

The treatment of 48 neurosyphilis patients with a form of pyrogen developed by the chemical laboratory of Northwestern University is reported. The drug, manufactured under the name of pyromen, produces fever comparable to malaria, typhoid, and other methods, and is less dangerous and less exhausting to the patients. Response was good.

ILLINOIS M. J., CHICAGO—CONTINUED

The management of vaginal discharges. Walter J. Reich and Mitchell J. Nechtow. Illinois M. J., 96:376-378, Dec. 1949.

A brief clinical discussion of the diagnosis and management of trichomonas vaginitis, monilial vaginitis, condylomata acuminata, and chronic cervicitis. Emphasis is placed on routine biopsy of all erosions and eversions prior to cauterization.

INDIAN M. GAZ., CALCUTTA

Syphilitic manifestations in the oral cavity. Arun Ganguli. Indian M. Gaz., 84: 335-337, Aug. 1949.

Two cases are reported.

J. PEDIAT., ST. LOUIS

Acute lymphocytic choriomeningitis. A study of twenty-one cases. William Roy Green, Lewis K. Sweet, and Rohert W. Prichard. J. Pediat., 35: 688-701, Dec. 1949.

Differential diagnosis of this condition is complicated by the fact that there are a host of conditions producing a serious meningitis quite similar clinically to that caused by the virus of lymphocytic choriomeningitis. In differential diagnosis (viral) lymphogranuloma venereum and (spirochetal) syphilis are the venereal diseases to be considered. Proof lies in isolation of the virus from the patient's blood or spinal fluid or demonstration of an increasing titer of antibody in the patient's blood following the acute illness.

J. SOCIAL HYG., NEW YORK

News from the States and communities.

District of Columbia: VD drive gets
underway. Esther Emerson Sweeney.

J. Social Hyg., 35: 389, Nov. 1949.

Thirty civic groups of the District of Columbia are participating in an intensive drive against venereal diseases in which the ultimate aim is distribution, into every Washington home, of venereal disease educational material in some form.

J. SOUTH CAROLINA M. A., FLORENCE

The purpuric state. Robert Wilson, Jr. J. South Carolina M. A., 45: 147-150, May 1949.

A study is reported of this condition, including the presentation of several

cases, two of which were due to administration of arsenicals for syphilis.

Pathological conference, Medical College of the State of South Carolina. Kenneth M. Lynch, Chairman. J. South Carolina M. A., 45: 380-382, 384, Dec. 1949.

Case of aneurysm which ruptured into the pulmonary artery, pathologic diagnosis being aneurysm, syphilitic, of aorta with compression and perforation of the pulmonary artery, the first of its type uncovered by the Department of Pathology.

J. THORACIC SURG., ST. LOUIS

The role of angiocardiography and venography in mediastinal and paramediastinal lesions. Osler A. Abhott, William A. Hopkins, and Ted F. Leigh. J. Thoracic Surg., 18: 869–898, Dec. 1949.

There is a definite place for use of venography and angiocardiography in the study of mediastinal and paramediastinal masses. Two cases are described where syphilitic aneurysms were demonstrated by angiocardiogram.

LANCET, LONDON

Penicillin in the cerebrospinal fluid. Joseph W. T. Redfearn, Alick Elithorn, Kenneth Till, and Frank A. Ibbott. Lancet, 2: 652-656, Oct. 8, 1949.

A total of 152 samples, some taken from patients with parenchymatous neurosyphilis, was assayed for penicillin. A single intramuscular dose of 0.5 megaunit produces a bactericidal cerebrospinal fluid-penicillin level in 70 percent of the patients. In addition, the penicillin penetrated tissue with damaged vascular structure more readily than normal tissue.

Ahortive treatment of venereal diseases. Lancet, 2: 900-901, Nov. 12, 1949.

The pros and cons of abortive treatment were discussed by the Medical Society for the Study of Venereal Diseases in England. It was thought that use of penicillin by mouth for prophylaxis was particularly dangerous because of irregular absorption, haphazard dosage, and inadequate treatment.

M. J. Australia, Sydney

The treatment of neurosyphilis. Eric Susman. M. J. Australia, 2: 829-831, Dec. 10, 1949.

M. J. AUSTRALIA—CONTINUED

Value of several therapeutic agents used in treatment of neurosyphilis is discussed. Treatment of choice is combination of penicillin and malaria.

The treatment of neurosyphilis. E. T. Hilliard. M. J. Australia, 2: 831–834, Dec. 10, 1949.

Several types of therapy employed in neurosyphilis are evaluated. Penicillin, fever, or pentavalent arsenicals may arrest the pathologic process of neurosyphilis within a year or more. Lack of associated clinical improvement in some patients is due to neurologic residuals of disease and type of psychosis present at time of treatment.

M. Officer, London

Female genital infection and the lavatory seat. W. McKim H. McCullagh. M. Officer, 82: 258, Dec. 17, 1949.

The author recommends open-front lavatory seats as a means of diminishing occurrence of such conditions as pediculosis pubis and trichomonas vaginitis.

M. Press, London

Modern treatment in psychiatry. L. C. F. Chevens. M. Press, No. 5763: 373-377, Oct. 19, 1949.

Penicillin is now employed in conjunction with fever and arsenicals in the treatment of general paresis. In early and late cases there is recovery in 25 to 30 percent, while 40 percent of the cases are arrested.

M. TIMES, NEW YORK

Infertility and fertility. [V. D.] Special Article. M. Times, 77: 395-405, Sept. 1949; 438-467, Oct. 1949.

A discussion is presented of treatment of vaginal infections, including trichomonas vaginitis and gonorrhea.

M. WORLD, LONDON

The recognition and treatment of vaginal discharge. Elliot Phillip. M. World, 71: 215–217, Oct. 7, 1949.

A discussion is presented of conditions causing vaginal discharge, including trichomonas vaginitis, syphilis, and gonorrhea. Clinical appearance, diagnosis, and therapeutic measures are considered.

Penicillin in syphilis. New preparations. M. World, 71:266, Oct. 14, 1949.

Administration, toxic reactions, and follow-up are reviewed briefly.

Aureomycin and chloromycetin. Ministry Announcements. M. World, London, 71: 460-461, Nov. 25, 1949.

Due to scarcity and high price, use of these drugs will be confined to treatment of specific conditions, including lymphogranuloma venereum.

MIL. SURGEON, WASHINGTON

Response of keratosis blennorrhagica to penicillin. W. W. Hiehle. Mil. Surgeon, 105: 211-215, Sept. 1949.

History of case complicated with polyarthritis, prolonged pyrexia, urethritis, and conjunctivitis is presented. Mild residuals were detected 6 months after discharge from hospital.

MISSISSIPPI DOCTOR, BOONEVILLE

Evaluation of the syphilis control program. Biloxi Area-Harrison County. Mississippi 1942–1948. Andrew Hedmeg and W. E. Frost. Mississippi Doctor, 27:268–272, Oct. 1949.

This article describes the syphilis control program.

NATURE, LONDON

Extraction of a specific antigen from the virus of lymphogranuloma venereum, Nature, 164: 1013, Dec. 10, 1949.

This study, in which it appears that acid treatment of the two viruses (psittacosis and lymphogranuloma venereum) carries into solution a specific antigen, which in that state or concentration can be demonstrated by its skin reactivity but not by complement fixation, is based upon the use of heated yolk sac suspensions.

NEW ENGLAND J. MED., BOSTON

Syphilis in pregnancy. A clinical study of factors responsible for congenital syphilis. Albert Heyman and John R. McCain. New England J. Med., 241:960-964, Dec. 15, 1949.

A study of records, from Grady Memorial Hospital in Georgia, of 77 women who delivered syphilitic infants in the past 4 years showed that factors chiefly responsible for transmission of syphilis to

NEW ENGLAND J. MED., BOSTON-CON.

the infants were lack of treatment as a result of negative serologic tests, and inadequate arsenical therapy.

NEW ZEALAND M. J., WELLINGTON

Canada's Federal health program. G. D. W. Cameron. New Zealand M. J., 48:454-460, Oct. 1949.

This paper, presented at the British Commonwealth Medical Conference, Saskatoon, June 1949, included a table of Provincial distribution of grants under the National Health Grants Program, fiscal year 1949–50, that of venereal disease amounting to \$515,944.

Public health in Japan. J. M. MacDonald. New Zealand M. J., 48:468-474, Oct. 1949.

Public health status is described. A law requiring premarital and prenatal examinations and examination of venereal disease contacts has been passed. Treatment is compulsory. More drugs are becoming available for therapy.

Condylomata acuminata. E. T. Dick and F. R. Duncanson. New Zealand M. J., 48:482-483, Nov. 1949.

The case presented is differentiated from the condylomata lata of syphilis.

PHILADELPHIA MED., LANCASTER

Neglect of V. D. wasteful. Philadelphia Med., 45:30, Aug. 13, 1949.

The director of public health urges all to make full use of facilities for diagnosis and treatment of venereal disease.

The Army reviews past year of medicine. Perfection of aluminum leg brace, further experiments with dramamine and reduction in V. D. cited. Philadelphia Med., 45:547, 549, Nov. 26, 1949.

The venereal disease rate is 58 percent ower than in 1946.

Modern treatment of infections. Penicillin and streptomycin. John A. Kolmer. Philadelphia Med., 45: 551-554, Nov. 26, 1949.

In a review of these antibiotics, the use of metals in the abortive treatment of syphilis is not acceptable, while approval is given to the use of penicillin in conjunction with bismuth and mapharsen, which was the basis of a study by Alexander in which the incidence was reduced from 62 percent to 5 percent.

Venereal disease control campaign under way. Richard A. Kern. Philadelphia Med., 45: 622, Dec. 10, 1949.

Letters to all Philadelphia physicians requested their cooperation.

PHYSICIAN'S BULL, INDIANAPOLIS

Penicillin in syphilis and other treponemal infections. Physician's Bull., 14: 162-167, Nov.-Dec. 1949.

A review of the literature is presented showing the early experience, present trends, and current investigation of the drug.

POSTGRAD. MED., MINNEAPOLIS

Syphilitic stenosis of the coronary ostia diagnosed during life. A. M. Gottlieb. Postgrad, Med., 6: 372-378, Nov. 1949.

A review is given of the diagnosis, treatment, pathology, and prognosis. Autopsy examinations indicate occurrence of the condition in 8.4 to 35 percent of cases of aortitis, which makes surprising its infrequent diagnosis by clinicians.

Practitioner, London

Penicillin in ophthalmology. [V. D.] Arnold Sorsby. Practitioner, 163: 194-199, Sept. 1949.

A study is presented of 400 cases of ophthalmia neonatorum and 24 cases of interstitial keratitis seen at the Ophthalmia Neonatorum Unit of White Oak Hospital. Schedules of treatment and results are described.

Advances in medicine. Clifford Wilson. Practitioner, 163: 257-265, Oct. 1949.

A summary is given of therapeutic advances made possible by the newer drugs.

PROC. ROY. Soc. MED., LONDON

Calcification of ascending aorta as a diagnostic sign of syphilitic aortitis. A. Elkeles. Clinical Section. Proc. Roy. Soc. Med., 42: 867-868, Nov. 1949.

A 54-year-old male showed enlargement of left ventricle, dilatation of ascending aorta with linear calcification 3 cm. in length at the right border, and positive Wassermann. Diagnosis was syphilitic aortitis.

Detection of linear calcification of the ascending aorta on radiographs raises suspicion of syphilitic aortitis.

PROC. SOC. EXPER. BIOL. & MED., UTICA

The treatment of *Trichomonas vaginalis* vaginitis with aureomycin. Leon V. Mc-Vay, Raymond L. Laird, James B. Flanagan, and Douglas H. Sprunt. Proc. Soc. Exper. Biol. & Med., 72: 674-675, Dec. 1949.

A powder for vaginal insufflation was prepared by adding aureomycin hydrochloride to powdered tale and insufflated into the vagina of 42 nonpregnant patients and 12 pregnant patients at the John Gaston Hospital, Memphis. Following insufflation, gelatin capsules of aureomycin were inserted into the vaginas. Results of treatment were satisfactory.

A substance in egg yolk which inhibits deterioration of aureomycin activity. C. Ray Womack, Edward H. Kass, E. Buist Wells, and Maxwell Finland. Proc. Soc. Exper. Biol. & Med., 72: 706-708, Dec. 1949.

A substance found in egg yolk inhibits deterioration of aureomycin activity which ordinarily occurs upon incubation at 37° C. The protective agent is heat stable and of sufficient concentration to permit dilution of egg yolk to 1:4 without significant diminution of aurcomycin-protective action. Egg albumen and human serum albumin are not protective in the concentrations used.

PSYCHIATRIC QUART., UTICA

A preliminary study on the hypnotizability of psychotic patients. [Syphilis.] C. Philip Wilson, H. H. Cormen, and A. A. Cole. Psychiatric Quart., 23: 657-666, Oct. 1949.

An attempt was made to test the hypnotizability of a random sample of 50 patients on the admission ward of a large State hospital. Included were 32 patients with organic psychosis, of whom 6 had central nervous system syphilis. Successful induction of hypnosis occurred in five of the central nervous system syphilis patients.

PSYCHOSOM, MED., NEW YORK

A formulation of the dynamics of the migraine attack. Robert M. Marcussen and Harold G. Wolffe. Psychosom. Med., 11: 251-256, Sept.-Oct. 1949.

A protocol is included from which it is inferred that cerebral damage resulting

from syphilis caused a change in personality structure and reactions which resulted in the elimination of migraine attacks. The personality was so altered as to prevent the development of the pernicious cycle which previously had led to headache.

QUART. J. STUD. ON ALCOHOL, NEW HAVEN

First admissions with alcoholic psychoses in New York State, year ended March 31, 1948. With a note on first admissions for alcoholism without psychoses. Benjamin Malzberg. Quart. J. Stud. on Alcohol, 10: 461–470, Dec. 1949.

In listing concomitant diseases, there were 15 cases of syphilis in males and 18 cases in females, the higher incidence in females being noteworthy.

Sc. News Lett., Washington

Aureomycin is successful in VD cases. S. News Lett., 56: 393, Dec. 17, 1949.

At the meeting of the American Medical Association in Washington, D. C., this drug was reported successful in treatment of all five venereal diseases and useful as a general prophylactic for them when taken by mouth.

SOUTH AFRICAN M. J., CAPE TOWN

Early syphilis. Some modern advances in its treatment with antibiotics with special references to chloromycetin, aureomycin and the "one shot" treatment with penicillin. R. R. Willcox. South African M. J., 23: 1040–1043, Dec. 24, 1949.

A review of the literature is presented.

UROL. & CUTAN. REV., WEST PALM BEACH

Renal and ureteral fistula of the visceral and cutaneous types. A report of four cases. Benjamin S. Abeshouse. Urol. & Cutan. Rev., 53: 641-674, Nov. 1949.

Included are descriptions of fistulas resulting from syphilis of the kidney. Pathology, prognosis, and treatment are also included.

V. D. H. J. Sims. Urol. & Cutan. Rev., 53: 704, Nov. 1949.

Historical data are presented on syphilis as it affects the central nervous system.

False positive diagnosis of gonorrheal cervicitis and urethritis produced by Aerobacter aerogenes; case report. Edward Eichner and Rosemary K. Ashe. Urol. & Cutan. Rev., 53:724, Dec. 1949.

UROL. & CUTAN. REV., WEST PALM BEACH— CONTINUED

Aerobaeter aerogenes from a vaginal discharge was mistakenly identified on smear and culture as Neisseria gonococcus. There was no response when the condition was treated as gonorrheal cervicitis with penicillin and diathermy.

Treatment of early syphilis with five day penicillin in oil and wax alone and combined with an arsenoxide derivative. John William Lentz. Urol. & Cutan. Rev., 53:732-736, Dec. 1949.

A study at Philadelphia General Hospital used two 5-day treatment schedules, penicillin in oil and wax alone and in combination with an arsenoxide derivative. Results revealed no advantage in the combined therapy.

Pharmacology of blood in psoriasis before and after therapy. David I. Macht. Urol. & Cutan. Rev., 53:736-742, Dec. 1949. Syphilitic serum is one of the pathologic serums employed in control experiments to check phygotoxic reaction.

WHO NEWSLETT., GENEVA

New plans against VD. WHO Newslett., No. 12:3, Nov.-Dec. 1949.

The Expert Committee on Venereal Infections met in Washington, D. C., during October 1949 and drew up a series of measures to strengthen health administration in various parts of the world in the fight against the venereal diseases. These measures are discussed.

WISCONSIN M. J., MADISON

Clinical evaluation of serologic tests for syphilis. Joseph M. Lubitz. Wisconsin M. J., 48: 988-990, Nov. 1949.

Serologic tests are discussed as to conflicting reports on the same blood, clinical syphilis with negative serologic reaction, significance of a doubtful reaction, false-positive reactions, seropositive reports without clinical syphilis, selection of serologic tests, and conflicting reports from different laboratories.

STATISTICS

Cases of Syphilis Reported to the Public Health Service by State Health Departments—Continental United States, 1943–49, by Color and Stage of Disease

[Known military cases excluded]

Colorjand_fiscal year	Total syphilis	Primary and secondary	Early latent	Late and late latent	Congenital	Not stated
White 1943 1944 1945 1946 1947 1948 1948	207, 895	31, 793	37, 620	104, 728	7, 438	26, 316
	169, 311	31, 539	31, 407	83, 437	6, 509	16, 419
	134, 120	30, 749	26, 005	61, 680	5, 436	10, 250
	141, 494	41, 547	30, 533	54, 482	5, 246	9, 686
	149, 461	46, 492	31, 493	54, 137	5, 461	11, 878
	127, 210	33, 215	26, 673	49, 873	5, 348	12, 101
	106, 475	21, 524	22, 705	50, 087	4, 883	7, 276
Nonwhite 1943	357, 023	50, 437	111, 289	148, 267	8, 735	38, 295
	288, 888	46, 879	90, 983	119, 159	7, 067	24, 000
	222, 195	46, 258	75, 130	81, 051	6, 903	12, 853
	219, 424	53, 410	76, 803	71, 354	6, 860	10, 997
	223, 835	60, 102	76, 262	68, 120	6, 823	12, 528
	210, 931	47, 313	71, 072	74, 099	7, 961	10, 486
	182, 294	32, 744	61, 637	71, 846	9, 412	6, 655

Source: Form 8958-B, FSA-PHS-Division of Venereal Disease.



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PUBLIC HEALTH SERVICE

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Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 10 cents. Subscription price: Domestic 75 cents a year; foreign \$1.15

Mass Screen Testing¹

E. M. Holmes, Jr., M. D., Paul W. Bowden, M. D., and James H. Stone 4

Introduction

Mass screen testing is a case-finding technic. It is a sensible approach to case finding; it is economical to the agency and to the taxpayer. Furthermore, the procedure is an effective approach, because the public is more readily attracted by the combination of tests.

Those of us who worked in some of the earlier public health case-finding procedures can profit from our mistakes. Public health leaders who made the early hookworm surveys in the southern States and those who later made the malaria prevalence studies learned from these case-finding efforts the basic technics of community education through demonstrable service. We learned that the problem of case follow-up is as important as case We discovered also the importance of the reaction of the newly discovered patient to his condition, to his treatment needs, and to his doctor. Later, when the Division of Venereal Disease of the United States Public Health Service attempted to collect venereal disease prevalence data, we learned how little information was available.

In the late twenties we learned from the early serologic survey work of Dr. O. C. Wenger ⁵ in one of the counties in Mississippi how effective a serologic dragnet could be. To his ability and enthusiasm we owe much of the success of our present knowledge of case-finding technics. It was through his work that the Julius Rosenwald Foundation of Chicago became interested in syphilis in the Negro

and agreed to finance studies in one county in each of six southern States; these studies stand not only as a landmark in syphilis control history but also as a monument to mass surveying.

In 1936, at the first National Venereal Disease Conference in Washington, nearly everyone agreed that mass blood testing was an effective case-finding procedure.

By 1938, interest in contact tracing was increasing, and health authorities were divided into two camps, one vehemently advocating blood-test surveys and the other emphasizing contact tracing. In retrospect, both of these technics were good and are still essential in a basic health program. The serologic testing procedures, the tracing of sex contacts, and education are just as vital to a syphilis control program as mass X-ray surveys, family contact investigations, and education are to the tuberculosis program. Today, through the influence of penicillin, new and increased impetus has been given to all syphilis case-finding technics. is still important to find all of the cases of syphilis existing in the population. Thus, we should by all means utilize the old serologic dragnet for syphilis in the new and popular multiphasic screening program. The advantages and reasons are many.

First, we are still not uncovering enough cases of early infectious syphilis. We must intensify our case finding through contact investigations, but we can still use the dragnet technic to advantage in locating cases as yet undiscovered by contact tracing.

Second, multitest programs bring people to examination who could not be attracted by a test for only one disease.

¹ From the Department of Public Health, Richmond, Va.

² Director.

³ Assistant Director.

⁴ Health Educator.

⁵ Formerly Director of the Hot Springs Venereal Disease Center.

⁶Albemarle County, Va.; Scott County, Miss.; Macon County, Ala.; Brunswick County, Ga.; Tipton County, Tenn.; and Pitt County, N. C.

They do respond, however, to the bait of testing for four or more conditions.

Third, the method is economical; the savings made through multitest procedures are tremendous. In some of the early serologic surveys for syphilis, we spent over a dollar per person tested. In the Richmond multiphasic testing program we are spending about \$1.12 per person tested, but we are now testing for nine conditions, not just one.

Fourth, community interest in health promotion activities is easier to stimulate and is no more expensive to launch than a similar single-test program. The interest of the public, of the medical society, and of health and health-related voluntary agencies in these programs is amazing.

The Richmond Program

The Richmond City Department of Public Health is now conducting a multiphasic screening program in which we hope to test 60,000 persons in the population within a 6-month period for the following conditions: syphilis, tuberculosis and other chest conditions, heart diseases, hypertension, anemia, diabetes, obesity, visual acuity, and intraocular tension. In addition, every tenth person is being given an electrocardiogram with 12 leads as a part of a special study. After trial runs, the program was opened officially to the public on January 3, 1950.

The cooperation that has been received from the Richmond Academy of Medicine, the State Department of Health, the voluntary health agencies, and the Richmond Area Community Council assured the success of this joint project of our department and the United States Public Health Service. While the project is under the official direction of the Richmond Department of Public Health, we are fortunate in having the support of the Health Division of the Richmond Area Community Council and the Academy of Medicine. Both of these agencies have appointed specialists in the various conditions to be tested for, and they act as a Medical Advisory Committee. It is through this committee and the staff of the United States Public Health Service that most of the technical difficulties have been worked out.

News releases, feature stories, donated newspaper advertising, radio, and word of mouth have provided excellent clinic promotion. The first two clinics were in large department stores, where over 12,000 persons were screened in the first 28 days of operation. Both stores provided liberal radio time and advertising space.

As the clinic moves into neighborhood and industrial areas, preceded by intensive promotional work, its structural setup will be revised to fit the new location. Later, the clinic will be broken down into two teams—one a mobile unit in a laboratory trailer and an X-ray truck, the other a portable unit that can be set up in small community buildings, etc.

Full-Time Employees

Twenty-nine employees devote their full time to this undertaking. Twenty-two work in the clinic proper, each one able to handle at least two assignments. Three are employed in the laboratory, and four are employed in the record room.

Clinic Employees

In charge of the clinic is a United States Public Health Service employee with a background of planning and running mass venereal disease screening programs. In addition, there are seven nurses, five technicians, seven Red Cross volunteers, and two typists.

There are five registered nurses. One of them is designated chief nurse, and she is in charge of supplies, rotation on relief, and position assignments. These nurses take blood pressures and blood specimens; they also cover positions at the hemoglobin-determination station, the height-and-weight station, the X-ray station, and any of the clerical stations. Three of the positions are paid through the multitest account, one is filled through the Richmond City Health Department, and one nurse is a volunteer from the staff of the Medical College of Virginia.

A public health nurse is stationed at the end of the line to collect the record from the individual and, while verifying this, to talk to him about any doubts he may have. She answers his questions and gives him various educational pamphlets. This nurse is assigned from the City Health Department or from the local Instructive Visiting Nurse Association staff.

Another nurse is able to cover any position in the line, and she serves as a floater to relieve other workers. At present she also fills the position of general technician.

The five specialized clinic technicians are: two cardiac technicians, two eye technicians, and an X-ray technician. These specialized technicians are the only ones without relief periods. The others relieve them by sending only half the accustomed number of patients to these stations for short periods. Including the floater nurse, two of these positions are paid through the multitest account, one is filled by the local Heart Association, and two are on United States Public Health Service cooperative budgets. The X-ray technician, a City Health Department employee, is paid a small extra stipend from the multitest account to develop films at night and on week ends.

Two typists fill in the basic information on the record form, one a City Health Department employee and one assigned from the Richmond Tuberculosis Association.

Seven positions are filled by Red Cross volunteers from the local chapter. The volunteers are used when the clinic is open to the public. They are essential to maintaining a smooth flow of individuals into the clinic line and from station to station. They also fill some of the nontechnical positions, permitting the other workers to double up at certain bottlenecks in the line when the load becomes heavy.

Laboratory Employees

The City Health Department Laboratory has taken on the entire load of serologic and urine examinations, as well as the maintenance of supplies. By working overtime and by using semitrained technicians to do preliminary preparatory work, they have managed to carry on with the addition of only two semitrained technicians and one washroom lielper. This would not be possible if the clinic were to be a permanent set-up or if the enthusiasm of the staff were not so high. Two of these employees are paid through the multitest account, and the other position is on a United States Public Health Service cooperative budget.

Record-Room Employees

The record-room staff consists of a statistical clerk assigned by the United States Public Health Service and three clerk-typists (two from the City Health Department and one paid through the multitest account). They record the results of laboratory tests and of X-ray and electrocardiogram reports, mail them to the physician, mail notices to the individuals tested, enter the physicians' reports on the final forms, and do the intermediate and final filing.

Part-Time Employees

In addition to the full-time employees, the Assistant Director and the Chief of Preventive Medical Services of the City Health Department do part-time work in a supervisory capacity. The Health Educators of the City Health Department and of the Richmond Tuberculosis Association spend most of their time in promotional work for the clinic and are also in charge of all scheduling. tuberculosis or chest clinic of the City Health Department and the four staff physicians of the City's sanatorium read all the X-ray films and reexamine all unsatisfactory or suspicious films. Two physicians of the Medical College of Virginia Cardiac Clinic interpret all the electrocardiograms. Many other

ployees of these agencies, as well as many local physicians, give essential, though part-time, service.

The flow of persons through the multitest clinic is handled efficiently. As the individual enters the reception room he is handed a numbered card and waits his turn. At the registration station, pertinent information and a medical history are taken, and the person being tested proceeds to the height-and-weight station. A 70-mm. chest X-ray is next taken, then his blood pressure. Blood specimens are taken for hemoglobin and for a serologic test for syphilis. An electrocardiogram and a visual-acuity test are offered to every tenth person. Every third person is offered an intraocular tension test. At the final station, each person is given a urine-kit container and health education materials. The public health nurse stationed here to answer questions sends him on his way in a happy frame of mind.

Between 60 and 70 persons an hour are screened. Although the average waiting is about 30 minutes, the actual screening time (not counting the electrocardiogram) takes 13 to 15 minutes.

The results of the laboratory tests are followed up through the private physicians. Normal as well as suspicious reports are mailed to the doctor whom the individual named, and later a postal eard is sent the individual informing him that his report has been mailed, giving the name of the doctor, and requesting that he arrange with his doctor to learn the results.

The physician interprets the findings, rechecking any that he feels are abnormal for the individual, and returns the record to the Health Department with his notation as to whether these results are normal or indicate pathology. In the latter event the physician gives his diagnosis and states whether the condition was previously known. These findings are then entered on all copies of the record.

Conditions such as syphilis and tuberculosis require such further field work by the Health Department as would normally take place if discovered through any other channel.

The project was financed chiefly out of the funds of the Health Department and the voluntary agencies. Table 1 contains an itemized break-down of the budget. If all services were included, as mentioned in footnote 3 (table 1), the budget would approximate \$97,000. The cost per examination is approximately \$1.12 per person tested if only the cash budget is

Table 1.—Budget for the Richmond mass screen-testing program

Grant-in-aid from the Public Health Service	\$13, 250, 00	
Supplementary grant, Public Health Service	7, 446, 00	
Cooperative salaries, Public Health Service	3, 450.00	
Total Federal funds		\$24, 166.00
Richmond Tuberculosis Association	22, 240. 90	
Richmond Heart Association	4, 600.00	
Richmond Red Cross	1 6, 900, 00	
Richmond City Health Department.	2 5, 058. 00	
Research Grant, State Health Department for Cardiac Program	4, 500.00	
Total local funds		43, 298. 90
Grand total		³ 67, 464, 90

¹ Volunteer services at rate of \$150 per month per person.

² Full-time salaries only. There is no allowance for part-time workers or for laboratory service or X-ray follow-up on suspicious or unsatisfactory 70-mm. X-rays.

³ It is estimated that the consulting services of the staff of the City of Richmond Department of Public Health and the Medical College of Virginia faculty in interpreting policies and in reading X-rays and electrocardiograms would cost an additional \$30,000 if the physicians and laboratory workers were paid for their services.

considered. If the entire budget, including allowance for consultation service, is considered, the per person cost would rise to \$1.62.

Summary

Among the expected benefits to be derived from the multitest clinic are:

- 1. Early indication of chronic diseases among many apparently well persons, with referrals to physicians for diagnosis and treatment.
- 2. Strengthening and further coordination of the related service and educational activities of the Health Department and of the voluntary health agencies.
- 3. Collection of data that will enable the Health Department to adjust its services according to greater needs, thus allowing better utilization of the tax dollar.

- 4. Provision of scientific data for use by the medical specialists and by some of the cooperating agencies.
- 5. Development of a closer relationship between patient, doctor, and community.

Early and thorough planning is essential in setting up a multiple-testing program. Nearly all of the technical and recording procedures can and should be thoroughly preplanned. Trial runs on a selected group are necessary to assure a smooth-running clinic, to estimate the volume of specimen-flow to the laboratory, to estimate the volume of patients, and to study timing.

Finally, we must work closely with the private physician, trying to render him a real service. We must provide laboratory service, consultation service with specialists in the particular field, and thorough case follow-up.

Crystalline Penicillin G Versus Amorphous Penicillin: Treatment of Early-Syphilis¹

George X. Schwemlein, M. D.,² Frederick Plotke, M. D., M. P. H.,³ and Jack Rodriquez, M. D.⁴

From June 1943 until the preparation of various pure fractions of penicillin, there have been numerous reports on the use of commercial amorphous penicillin in the treatment of early syphilis. This amorphous penicillin has been a changing

mixture of various substances. The composition as regards the several identified penicillin fractions, G, F, X, and K, has been quantitatively variable. These changes have suggested that therapeutic efficacy may not have remained constant. It may be that the results of the earlier investigations are not comparable to those of today. Since the production and clinical use of crystalline penicillin G, it is possible to appraise the extent to which these ever changing penicillin fractions in the amorphous penicillin may have affected the earlier investigations.

All the patients included in comparative studies are of the darkfield-positive secondary syphilis category. Statistical methods of evaluation of results are identical.

In the present investigation, data are

¹ From the Chicago Intensive Treatment Center, Venereal Disease Control Program, Chicago Board of Health, in cooperation with the U. S. Public Health Service. Under the direction of Herman N. Bundesen, Senior Surgeon (R) (Inactive), U. S. Public Health Service; President, Chicago Board of Health.

² Research Associate, Kettering Foundation for Medical Research, Cincinnati; Instructor, Department of Internal Medicine, College of Medicine, University of Cincinnati.

³ Venereal Disease Control Officer, Chicago.

⁴ Medical Director, Chicago Intensive Treatment Center; Research Associate, Kettering Foundation for Medical Research, Chicago.

presented on the use of total dosages of 2.4 million units of crystalline penicillin G administered in aqueous solution—40,000 units intramuscularly every 3 hours over a period of 7½ days for 60 injections.

One hundred and seventy-one patients with darkfield-positive syphilis were treated by the described schedule of treatment from August 12, 1946, through October 30, 1947. No further treatment was administered unless either clinical or serologic relapse occurred. The results of observation of these patients over a maximum period of 38 months and a minimum period of 23 months are presented.

The distribution of patients by race, sex, and age is indicated in table 1. The

Table 1.—Number of patients treated with 2.4 million units of penicillin G in 60 injections during 7½ days, grouped by race, sex, and age

Race and sex	Age in years					
	Total	Under 20	20-24	Over 24		
Total Male Female	170 125 45 22	17 8 9	67 50 17	86 67 19		
White Male Female	18 4		8 8	- 14 10 4		
Negro Male Female	148 107 41	17 8 9	59 42 17 .	72 57 15		

ages of the patients ranged from 17 to 46 years: 9.9 percent were under 20 years; 39.2 percent were from 20 to 24 years; and 50.9 percent were 25 years and over.

There were 35 (20.5 percent) cases of primary seronegative syphilis; 56 (32.7 percent) cases of primary seropositive syphilis; 79 (46.2 percent) cases of secondary syphilis; and 1 (0.6 percent) case of relapsing secondary syphilis, which has been excluded from the tabulations.

One hundred and sixty-one patients had received no previous treatment; 10 patients had received some type of antisyphilitic treatment prior to their present hospital admission, but had been subsequently reinfected or had evidenced re-

lapse or inadequate resolution of their lesions. The previous treatment had consisted of arsenicals, penicillin, bismuth, and fever therapy alone or in various combinations over short and long periods.

The results of treatment are summarized in table 2 and demonstrated graphically in figure 1.5 The cumulative failure rate in the 12–15 months' observation period was 12.0 percent for 35 patients with primary seronegative syphilis; 19.4 percent for 56 patients with primary seropositive syphilis; and 15.6 percent for 79 patients with untreated secondary syphilis. The over-all failure rate, regardless of diagnosis, was 16.2 percent.

Of 136 patients with positive pretreatment serologic titers, 106 (77.9 percent) reversed to negative. Fifty-six patients (41.2 percent of the 136) were negative by the end of the first 3 months, and 95 (69.9 percent) were negative within 6 months. All but 2 of the 106 patients had become negative within the first year—one had a doubtful Kahn test, and the other had a 3-unit positive Kahn test. The median number of days required to reach seronegativity was 58 f for 46 patients with primary syphilis and 115 for 63 patients with secondary syphilis. Eleven patients (10.4 percent of the 106 who reached seronegativity) were later re-treated—2 for clinical relapse, 4 for serologic failure, and 5 as reinfections.

Cerebrospinal fluid examinations were made for all patients—124 before treat-

⁵ The percentages used for the figures on successes and failures were obtained by assuming that patients lost from observation would have shown the same ratio of results of treatment as those observed. The ratio of the number of patients observed in each period to the number observed in the preceding period was applied to the cumulative failure figure. Patients with positive significant titers (4 Kahn units or more) after 12 to 15 months' observation have been grouped with failures. Those who were seronegative or who maintained nonsignificant titers (3 Kahn units or less) were, for the present, considered successes. This method of evaluation is considered rigid, and as a consequence, the failure rate tends to be relatively higher than in similar studies utilizing less rigorous criteria.

⁶ Data biased by irregularity of follow-up.

Table 2.—Number of patients treated with 2.4 million units of penicillin G in 60 injections, during 7½ days, grouped by number of days of observation and treatment results

	Number of patients					
Number of days from beginning date of therapy	Total observed	Serologic titer		Failures found during period		
	during period or later	Negative	Positive	Reinfec- tions	Relapses	
0-29	170	36	134			
30-59	158	63	93		2	
60-89	156	84	68	1	3	
90-119	149	102	42	1	4	
120-149	141	110	28	1	2	
150-179 180-209	135 130	112 111	22 19		,	
	129	116	19	<u>-</u>		
210-239 240-269	124	115	8	·	1	
270-299	100	114	6			
300-329		113	3			
330-359		110	4			
360-449	113	108	4	1		



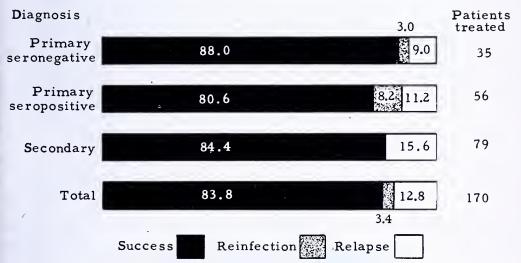


FIGURE 1.—Darkfield-positive primary and secondary syphilis patients treated with 2,400,000 units of aqueous crystalline penicillin G (40,000 units every 3 hours for 60 injections in 7.5 days). Cumulative percentages of successes and failures, 12 to 15 months' observation.

ment and 47 during treatment. Findings were normal ⁷ for 145 patients (84.8 percent of the total 171). Posttreatment cerebrospinal fluid examinations were made for 47 of these 145 patients: 1

patient had doubtful Kahn and negative Eagle tests; 1 showed 17 lymphocytes; a third showed 49 mg. total protein; while the balance of 44 remained normal. For 26 patients (15.2 percent) pretreatment findings were abnormal—3 in cell count only and 23 in total protein, ranging from 46 mg. to 90 mg. Of 15 patients later reexamined, 10 had reversed to normal (in-

⁷Criteria for normal cerebrospinal fluid: Kahn, negative; cell count, 7 lymphocytes or less; total protein, 45 mg. percent or below; colloidal gold test, negative.

cluding 2 patients re-treated for clinical relapse), and 4 showed an improved cerebrospinal fluid formula; 1 showed asymptomatic neurosyphilitic progression.

Of the 171 patients treated, 26 were classified as failures-23 by the 12 to 15 months' observation period and 3 after a longer period. Sixteen failed following treatment for primary syphilis, and 10 failed after treatment for secondary syphilis. The former included 6 patients with relapsing primary syphilis; 3 with primary syphilis progressing to secondary syphilis, 2 serologic relapses, and 5 reinfections. The latter included 3 patients with relapsing secondary syphilis, 5 serologic relapses, 1 neurorecurrence, and 1 reinfection. Of the 3 failures occurring after the fifteenth month, 1 was a serologic relapse, and 2 were reinfections.

There were no serious complications resulting from the treatment administered. Fifty-six patients of the total 171 demonstrated mild to moderate febrile Herxheimer reactions. Seven patients had cutaneous Herxheimer manifestations.

Comment

Two methods of treatment employed in sizable numbers of cases of darkfield-positive secondary syphilis at this center are worthy of comparison: (1) the method described in this investigation, employing aqueous solution of crystalline penicillin G every 3 hours for 60 intramuscular injections; and (2) that used in a previous study, employing amorphous penicillin (fraction amounts of G, F, X, and K unknown) on the same time-dosage basis (1).

When 266 secondary syphilis patients were given 2.4 million units of amorphous penicillin in 7½ days (1944-45), the cumulative failure rate was 26.8 percent (including reinfections) at the end of 12 to 15 months. In 1945-46 this same type of penicillin was spread over a 15-day period (20,000 units for 120 injections) in 63 secondary syphilis patients, and the failure rate was 24.2 percent, showing no significant difference in the two amorphous penicillin schedules when the treatment period was doubled.

However, in the study described, 79 patients with secondary syphilis were

12 - 15 Months' Observation

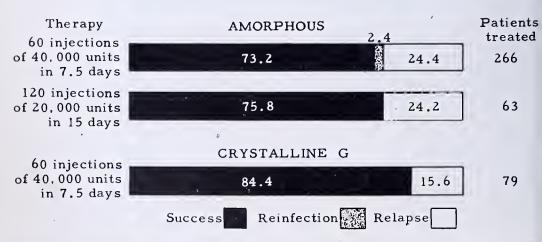


Figure 2.—Darkfield-positive secondary syphilis patients treated with 2,400,000 units of amorphous penicillin or crystalline penicillin G. Cumulative percentages of successes and failures, 12 to 15 months' observation.

given crystalline penicillin G (40,000 units for 60 injections in $7\frac{1}{2}$ days), and the failure rate was 15.6 percent (fig. 2).

It is indicated by this study that, in the treatment of early syphilis, crystalline penicillin G is therapeutically more effective than the amorphous penicillin employed at this center.

Summary

1. One hundred and seventy-one patients with darkfield-positive primary and secondary syphilis were each given 2,400,000 units of crystalline penicillin G over a period of 7½ days.

- 2. The cumulative failure rate, regardless of diagnosis, at the end of the 12–15 months' observation period was 16.2 percent.
- 3. Data are presented to show that crystalline penicillin G is therapeutically more effective than amorphous penicillin in the treatment of early syphilis.

Reference

1. Bundesen, H. N.; Plotke, F.; Schwem-Lein, G. X.; Rodriquez, J.: Penicillin in the treatment of early syphilis: 639 patients treated with 2,400,000 units of sodium penicillin in 7½ days. J. Ven. Dis. Inform., 30: 321-325, November 1949.

Adaptation of the VDRL Method for Total Protein Determination to the Use of Small Quantities of Cerebrospinal Fluid¹

Rudolph K. Waldman, Dr. Chem., Lorraine F. Ullrich, A. B., and Earle K. Borman, M. S.

The fact that the original VDRL turbidimetric method (1, 2, 3) for the quantitative determination of total protein content of cerebrospinal fluid calls for the use of 2.5 ml. of each specimen presents an obstacle to its routine use when specimens received are too small in volume for the performance of this test in addition to serologic tests for syphilis and colloidal gold or similar tests. This has constituted a real problem in our laboratory and probably in other State health department laboratories. though the authors of this method state that reduced test volumes can be used

This report is made to call attention to a successful attempt to adapt the VDRL method for use on small quantities of fluid without resort to expensive, specially designed cuvettes for the type of spectrophotometer which was available to us. This was a Coleman Universal, model 11, with which we found it convenient to use matched test tubes, 19 mm. x 150 mm., as cuvettes, reading final turbidities with reference to light transmission at 420 m μ wave length (filter PC4). Calibration charts used for conversion of percent transmission to protein concentration were plotted from

provided relative proportions of fluid and reagent are kept constant, any reduction in final test volume is limited by the adaptability of the available photoelectric instrument to the use of small cuvettes.

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² Principal Biochemist.

³ Assistant Biochemist.

⁴ Assistant Director of Laboratories.

measurements on known concentrations of serum proteins over the range 20 mg. to 200 mg. per 100 ml. (appropriately spaced at 10 mg. to 20 mg. steps), prepared by dilution of Kjeldahl-analyzed material after treatment according to the technic under trial.

Modification of the Method

Our first problem was to determine whether or not fluids of normal protein content could be tested satisfactorily in a final dilution of 1:10 or 1:20 instead of the 1:2 final dilution used in the original method.

An early observation while working with concentrations of protein in the lower portion of the range was the rapid settling of the protein which occurred after mixing with trichloracetic acid, necessitating special care in resuspending the particles immediately before reading; this often resulted in the inclusion of interfering bubbles of air. To overcome this difficulty, several agents were tried as stabilizers for the suspended protein precipitate and Methocel was chosen as the most suitable.

Preparation of the Methocel stabilizer is as follows:

- 1. Weigh out 10 gm. of Methocel of 1,500 cps. viscosity,⁵ and cut it into small shreds; place shredded Methocel into a 2-liter beaker.
- 2. Measure out 1 liter of distilled water, of which heat 200 ml. to 300 ml. to boiling; add the boiling water to the shredded Methocel; stir with a glass rod.
- 3. Place beaker and contents (with stirring rod) in refrigerator; place remainder of distilled water in refrigerator in separate container.
- 4. When both have chilled thoroughly, pour the cold distilled water upon the Methocel gel, and mix thoroughly by stirring and pourling from one container to the other.
- 5. Finally, dilute this preparation with 1 liter of distilled water, mix, and store reagent in refrigerator.

After numerous trials, the following modification of the VDRL method has been adopted for routine use:

- 1. Select for testing only those cerebrospinal fluids which are without visible turbidity due to bacterial contamination, presence of cells, or other cause.
- 2. Centrifuge fluids to sediment chance particles invisible to the eye, and decant supernatant carefully for use in the test.
- 3. Use optically matched test tubes, 19 mm. x 150 mm., for initial adjustment of instrument and for testing. Periodically inspect matched tubes for scratches, etc., which will change light transmission; check individual tubes in the spectrophotometer when in doubt.
- 4. Place test tubes, specimens, and reagents in clear water in a 37° C. bath to equalize them at that temperature. Bottles of reagent may have to be held in the bath for as long as 1 hour prior to testing, depending upon the volume in each container.
- 5. Into a test tube, pipette 0.5 ml. of clear specimen, 1.5 ml. of 10-percent trichloracetic acid, and 7.0 ml. of Methocel. Mix by inversion and allow to stand in a 37° C. bath for at least 30 minutes. Remove tubes from bath and allow water to drain from outer surfaces. Just before reading, wipe surface of each tube with clean lintless tissue or soft cloth.
- 6. With wave length of 420 m μ (filter PC4), adjust spectrophotometer (Coleman Universal, model 11) to reading of 100 percent transmission with tube containing mixture of 0.5 ml. of distilled water, 1.5 ml. of 10-percent trichloracetic acid, and 7.0 ml. of Methocel.
- 7. With spectrophotometer thus adjusted, read percentage transmission of light for each specimen under test.
- 8. Refer to previously prepared calibration chart to convert percentage transmission to milligrams protein per 100 ml. As stated previously, this calibration

⁵ Dow Chemical Co.

⁶ Rotation of a given test tube may cause variations in light transmission; therefore, an etched vertical line on the upper portion of each tube furnishes an easy reference point for orienting the tube in the light path.

chart is prepared by measurements of light transmission through serum protein dilutions of known Kjeldahl-controlled concentrations over the range of 20 mg. to 200 mg. per 100 ml. after treatment by the method described above. practice, we have used a minimum of five separate readings obtained on five duplicate portions of each serum protein dilution to obtain values for the calibration chart. Within the range specified, the relationship between known concentrations and their respective percents transmission can be expressed as a straight line graph on ordinary graph paper, all values falling within the range of 30 percent to 90 percent transmission.

Discussion

One advantage of this method, resulting from using small quantities of fluid with an excess of reagent and stabilizer, is elimination of the necessity for diluting fluids when protein values rise above 100 mg. per 100 ml. In practice, we report the occasional specimen which contains over 200 mg. simply as "more than 200 mg. per 100 ml."

Tempering of all reagents to 37° C. before use in the test is stressed for reasons of accuracy. The influence of temperature has been reported by Harding and Harris (3). If temperatures are not carefully controlled, calibration charts prepared from readings on standard proteins precipitated at room temperature will result in variable errors throughout the range of room temperatures at which unknown proteins may be tested throughout the year. For example, with the spectrophotometer calibrated at 20° C. we have made a series of duplicate tests on fluids at 20° C. and at 37° C. The average apparent but false increase in results at the higher testing temperature on 18 fluids was 25 percent, and the discrepancy on some individual specimens of low protein content approached 100 percent. These discrepancies, due to differences in particle size of precipitated proteins, call for careful temperature control, and we concur in the selection of 37° C. as a suitable and the most convenient temperature for precipitating the proteins including the serum standards used to calibrate the instrument. We have found that it is also desirable to temper reagents at 37° C. before mixing to avoid a further source of error. We have finally recommended that test tubes stand in the bath for 30 minutes before reading because after that time no change occurs in particle size of precipitate when the tubes cool, so that they may be removed from the bath after 30 minutes to allow drying of the water on the outer surface of the tubes at room temperature before reading. Coagulated proteins do not settle out readily because of the stabilizing effect of the Methocel and, consequently, no further mixing of the contents of tubes is necessary if readings are made within 2 to 3 hours.

Summary

Because of limitations imposed amounts of cerebrospinal fluid specimens received in a State laboratory and by the apparatus available, a modification of the VDRL method for total protein content has been devised which makes use of 0.5 ml. of specimen and of optically matched test tubes of a standard size with the Coleman spectrophotometer, model 11. firming the results of others, the effect of temperature on particle size of proteins precipitated by trichloracetic acid has lead to recommendations that precipitation be carried out at a readily controlled temperature—37° C. To obtain sufficient volume in the tests and to retard settling of precipitated proteins, a protective colloid sol (Methocel) is recommended.

References

- 1. Bossak, H. N.; Rosenberg, A. A.; Harris, A.: A quantitative turbidimetric method for the determination of spinal fluid protein. J. Ven. Dis. Inform., 30:100-103, April 1949.
- Manual of Serologic Tests for Syphilis. Supplement No. 22 to J. Ven. Dis. Inform., 1949. Pp. 117-118.
- 3. Harding, V. L.; Harris, A.: The effect of temperature variants on quantitative turbidimetric determinations of spinal fluid protein, using trichloracetic acid.
 J. Ven. Dis. Inform., 30:325-327, November 1949.

CURRENT NOTES AND REPORTS

University of Pennsylvania Offers Summer Course

The University of Pennsylvania has announced the Eighth Annual Course in Family Living and Sex Education to be held from June 26 to July 28, 1950. It is being presented by the School of Education and the Institute for the Study of Venereal Disease under the sponsorship of the United States Public Health Service, the American Social Hygiene Association, the Pennsylvania State Department of Health, the University of Pennsylvania, and the Philadelphia Board of Public Education.

The course is being given in five units, with a chairman for each area: The Family—Professor James H. S. Bossard, Department of Sociology; Child Guidance—Frederick H. Allen, M. D., Department of Psychiatry and Philadelphia Child Guidance Clinic; Public Health Aspects—Nor-

man R. Ingraham, Jr., M. D., School of Medicine and Department of Public Health of Philadelphia; Educational Practices—Howard L. Conrad, Principal, Mayfair School, Philadelphia Board of Public Education; Community Responsibilities—Robert C. Taber, Director of Pupil Personnel and Counseling, Philadelphia Board of Public Education. The discussion leader will be Mrs. Elizabeth Force, Counselor, Toms River Schools, New Jersey. There will be a faculty of 45 associates and visiting speakers.

The 5-week summer course is planned primarily for teachers, counselors, social and public health workers. Full information is available from Dr. John H. Stokes, University of Pennsylvania, 34th and Locust Streets, Philadelphia 4, Pa.

CURRENT LITERATURE

ALASKA'S HEALTH, JUNEAU

Premarital and prenatal laws explained.
Alaska's Health, 7: 1, 4, July-Aug. 1949.
On June 17, 1949, Territorial laws requiring a standard blood test before marriage and for the expectant mother went into effect.

AM. J. CLIN. PATH., BALTIMORE

Preliminary note on occurrence of a fraction in soya bean scrologically active in cases of syphilis. Gwen M. Macnab. Am. J. Clin. Path., 20:61-63, Jan. 1950.

A fraction derived from the soya bean when mixed with an extract of egg yolk was serologically active in cases of syphilis. Results are given of tests with the experimental material when used according to the technics of the Kahn precipitation, modified Ide precipitation, Eagle flocculation, and Kolmer complement-fixation procedures.

AM. J. NURSING, NEW YORK

Modern venereal disease control. Nels A. Nelson. Am. J. Nursing, 50: 75-77, Feb. 1950.

Control work is discussed as to objectives and the nurse's place in the program.

AM. J. OBST. & GYNEC., St. Louis

The bactericidal action of beta progesterone. Marie L. Koch. Am. J. Obst. & Gynec., 59: 168-171, Jan. 1950.

A report is made of the effect upon viability of genus *Neisseria*, particularly gonorrhea, making use of nine strains with dilution showing no growth after incubation at 37° C.

Treatment of granuloma inguinale with streptomycin. Charles R. Freed and Franklin M. Kern. Am. J. Obst. & Gynec., 59: 195-199, Jan. 1950.

Six patients were successfully treated at University of Pennsylvania Graduate

Am. J. Obst. & Gynec.—Continued

Hospital with a dosage of 20 gm. in 1-gm. doses intramuscularly every 6 hours.

AM. J. OPHTH., CHICAGO

Gummas of the eyelid. J. V. Cassady. Am. J. Ophth., 33: 18-22, Jan. 1950.

Review of literature reveals that the condition is uncommon. A case is presented which shows a resemblance to a chalazion.

Choroiditis proliferans. The Charles H. May lecture. Adalbert Fuchs. Am. J. Ophth., 33: 69-76, Jan. 1950.

This new type of fundus disease occurs more frequently than is generally assumed. The first case described in 1943. Pathology included hereditary syphilis.

AM. J. PSYCHIAT., NEW YORK

Neurosyphilis. Review of psychiatric progress 1949. Augustus S. Rose. Am. J. Psychiat., 106: 522-524, Jan. 1950.

Penicillin in treatment of neurosyphilis is reviewed. Though aureomycin shows slow action in treatment of early syphilis, its use in central nervous system syphilis is doubtful. Oral administration may offer hope for newer and better antisyphilitic agents and methods of treatment in the future.

AM. J. PUB. HEALTH, NEW YORK

Significance of UNICEF's role in international child health activities. P. Z. King. Am. J. Pub. Health, 40: 177-182, Feb. 1950.

Venereal disease control is discussed as one phase of the emergency program.

AM. J. SURG., NEW YORK

Granulomatous rectal stricture. Clinical response to ethylstilbesterol. F. George Rebell and Fred E. Bradford. Am. J. Surg., 79: 213–217, Jan. 1950.

Patients in this study, selected from the Proctologic Services of the Los Angeles County General Hospital and White Memorial Clinic, responded in a manner superior to that of any other remedy.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

Hyaluronidase and experimental syphilis.

I. The length of incubation periods in experimental primary syphilis with and without hyaluronidase. Virgil Scott and

Clarence Droegemueller, Am. J. Syph., Gonor. & Ven. Dis., 34: 1-11, Jan. 1950.

Results of three experiments are described. Incubation periods of primary lesions resulting from intradermal inoculation of *Treponema pallidum* obtained from lymph nodes with and without addition of hyaluronidase were studied. Results suggest that addition of hyaluronidase effects a shortening of incubation period. Study was done at Washington University, St. Lonis.

Hyaluronidase and experimental syphilis. II. The attempted localization of lesions in syphilitic rabbits by intradermal and by intracorneal injections of hyaluronidase. A negative report. Virgil Scott. Am. J. Syph., Gonor. & Ven. Dis., 34: 12-17, Jan. 1950.

Localization of lesions was not produced in rabbits with syphilis of varying duration by injection of hyaluronidase. Study was done at Washington University, St. Louis.

The effect of the method of inoculation upon the course of experimental syphilis in the rabbit. Alan M. Chesney and Gerald J. Schipper. Am. J. Syph., Gonor. & Ven. Dis., 34: 18-24, Jan. 1950.

Three groups of adult Chinchilla rabbits were inoculated with equal amounts of virulent syphilitic virus, one group being inoculated intracutaneously, another intravenously, while the third was inoculated intratesticularly. Course of infection was observed for 85 days. The incidence of generalized lesions was greatest in animals inoculated intravenously and least in those inoculated intracutaneously. Study was done at Johns Hopkins University.

The effect of the method of inoculation on the behavior of the serologic test for syphilis in experimental syphilis of the rabbit. Gerald J. Schipper and Alan M. Chesney. Am. J. Syph., Gonor. & Ven. Dis., 34: 25-33, Jan. 1950.

Three serologic tests were performed on three groups of rabbits inoculated intracutaneously, intratesticularly, and intravenously. Reactions obtained with the tests reached their maximum degree of positivity about the eightieth day. Highest degree of positivity was in the group inoculated intravenously, while the

AM. J. SYPH., GONOB. & VEN. DIS.—Con. lowest was in those inoculated intracutaneously. Study carried on at Johns Hopkins University.

Electron microscope studies of treponemes. II. The effect of penicillin on the Nichols strain of *Treponema pallidum*. Harry E. Morton and John Oskay. Am. J. Syph., Gonor. & Ven. Dis., 34: 34-39, Jan. 1950.

In the presence of subspirochetostatic concentrations of penicillin G in vitro, cells of Nichols strain of *Treponema pallidum* showed a lengthening of individual cells, tendency for incomplete fission so that chains of as many as six treponemes were observed, and an occasional increase in transverse diameter of cells. Penicillin did not appear to suppress the fiagella-like processes of the treponemes, nor were buds, lateral or terminal, and tightly coiled masses of treponemes observed.

Experimental mouse syphilis. II. Minimal infectious number of *Treponema pallidum*. Paul D. Rosahn and Catharine L. Rowe. Am. J. Syph., Gonor. & Ven. Dis., 34:40-44, Jan. 1950.

Mice were inoculated intraperitoneally with *Treponema pallidum* varying from 25,000 to 5 million organisms. Following incubation of 10 to 13 and 81 to 92 days, lymph nodes from inoculated mice were subinoculated intratesticularly into rabbits. Minimal number of organisms in original inoculum capable of producing lesions in rabbits at 10 to 13 days was 1 million, and at 81 to 92 days, it was 100,000.

The treatment of acute syphilitic orchitis and generalized syphilis of rabbits with repository penicillin products alone and in combination with mapharsen and bismuth salicylate. John A. Kolmer. Am. J. Syph., Gonor. & Ven. Dis., 34: 45–56, Jan. 1950.

Four repository penicillin compounds (penicillin G sodium in refined peanut oil and bleached beeswax, procaine penicillin G in aqueous suspension, procaine penicillin G in sesame oil, and procaine penicillin G in refined peanut oil with 2 percent aluminum monostearate) were employed in 8- and 15-day treatment schedules. Procaine penicillin G was approximately as therapeutically effec-

tive as penicillin G sodium suspended in peanut oil and bleached beeswax. Mapharsen by intravenous injection and bismuth salicylate in oil by intramuscular administration possessed as much synergistic activity with the three procaine penicillin G products as penicillin G sodium in peanut oil and beeswax.

Revised criteria of cure in gonorrhea. Adolph Jacoby and Theodore Rosenthal. Am. J. Syph., Gonor. & Ven. Dis., 34: 57-59, Jan. 1950.

New York City Health Department Clinics have proposed limitation of post-treatment examinations to a single smear and culture made within 7 days after treatment and to discharge patients negative on this examination. Loss by omitting further examinations can be assumed without serious detriment to control efforts.

Treatment of gonorrhea with oral penicillin. Adolph Jacoby and Arthur H. Ollswang. Am. J. Syph., Gonor. & Ven. Dis., 34: 60-61, Jan. 1950.

Percentage of cures obtained with doses ranging from 400,000 to 600,000 units indicated that oral therapy will prove to be a practical, painless, and satisfactory therapeutic procedure. Results on 293 patients are shown in tables. Work was done by Department of Health, New York City.

The use of dihydrostreptomycin in the treatment of gonorrhea. S. R. Taggart, D. E. Putnam, A. B. Greaves, and J. A. Watson. Am. J. Syph., Gonor. & Ven. Dis., 34: 62-63, Jan. 1950.

A report of 104 patients treated by the District of Columbia Health Department with 0.2 to 0.4 gm. dihydrostreptomycin showed a cure in 95 cases. Criteria of cure were the disappearance of symptoms and at least one negative culture.

Aureomycin in the treatment of gonorrhea in the male. Raymond C. V. Robinson. Am. J. Syph., Gonor. & Ven. Dis., 34:64-66, Jan. 1950.

In a study at Johns Hopkins Hospital, a single dose of 1.0 gm. was found to cause disappearance of urethral discharge in 56 of 70 patients.

Treatment of lymphogranuloma venereum with aureomycin. Raymond C. V. Robin-

AM. J. SYPH., GONOR. & VEN. DIS.—Con. son, Harold E. C. Zheutlin, and E. Randolph Trice. Am. J. Syph., Gonor. & Ven. Dis., 34: 67-70, Jan. 1950.

Only three of nine patients treated at Johns Hopkins Hospital with dosages of 0.56 to 3.6 gm. intramuscularly in 4 to 15 days or 3.6 to 38.0 gm. orally in 5 to 15 days showed any definite improvement.

Aureomycin in the treatment of chancroid:
A report of three cases. Harold E. C.
Zheutlin and R. C. V. Robinson. Am. J.
Syph., Gonor. & Ven. Dis., 34:71-72, Jan.
1950.

Patients were successfully treated at Johns Hopkins Hospital in daily doses of 2 gm. over a period of 7 to 14 days.

Seropositivity in patients previously treated for syphilis. The differentiation between seroresistance and "treatment failure." Ira Leo Schamberg. Am. J. Syph., Gonor. & Ven. Dis., 34: 73-77, Jan. 1950.

Six factors of value in a differential diagnosis are presented along with five case histories illustrating the problem.

Fatal Herxheimer reaction following penicillin therapy. Report of a case of syphilitic pachyleptomeningitis. Bertram Shaffer and Henry A. Shenkin. Am. J. Syph., Gonor. & Ven. Dis., 34: 78-82, Jan. 1950.

Death occurred 10 days following institution of therapy.

Donovanosis—granuloma inguinale. Incidence, nomenclature, and diagnosis. Milton Marmell and Edward Santora. Am. J. Syph., Gonor. & Ven. Dis., 34: 83-90, Jan. 1950.

Authors suggest donovanosis as name for disease caused by Donovan bodies. Of 70 patients at Rikers Island Hospital, New York, with anogenital lesions, 15 were diagnosed as having donovanosis. Case histories of these are described.

ARCH. DERMAT. & SYPH., CHICAGO

Penicillin in the treatment of experimental syphilis of rabbits. V. The synergistic or additive activity of penicillin injected intramuscularly with sodium iodide administered orally and intravenously. John A. Kolmer. Arch. Dermat. & Syph., 61: 49-55, Jan. 1950.

The minimal curative dose of penicillin given intramuscularly twice daily for 8 days for treatment of acute syphilitic orchitis of rabbits was 500 units per kilogram per dose for a total of about 8,000 units. Sodium iodide in a dose of 0.025 to 0.100 gm. per kilogram intravenously twice daily for 8 days for a total of 0.4 to 1.6 gm. per kilogram was slightly spirocheticidal but not completely curative. It appeared that penicillin and iodides act synergistically or additively in treatment of experimental syphilis.

Penicillin in the treatment of experimental syphilis of rabbits. VI. The synergistic or additive activity of penicillin injected intramuscularly and tryparsamide administered intravenously. John A. Kolmer. Arch. Dermat. & Syph., 61:56-62, Jan. 1950.

The single minimal curative dose of commercial penicillin intramuscularly in isotonic solution of sodium chloride in treatment of acute syphilitic orchitis was approximately 200,000 units per kilogram of body weight. The minimal curative dose of tryparsamide intravenously was about 0.6 gm. per kilogram of body weight. The intravenous injection of 0.05 gm. of tryparsamide per kilogram had no appreciable synergistic or additive spirocheticidal effects on the single minimal curative dose of penicillin injected intramuscularly. It appeared that combined treatment with penicillin and tryparsamide showed some degree of synergistic or additive spirocheticidal activity but not as pronounced as penicillin combined with mapharsen or bismuth.

Treatment of syphilis with aureomycin administered by mouth. Robert R. Kierland, Wallace E. Herrell, and Paul A. O'Leary. Arch. Dermat. & Syph., 61: 185-195, Feb. 1950.

Seven patients with early infective syphilis, late cutaneous lesions, or neuro-syphilis were treated at Mayo Clinic with total oral dosages ranging from 44.2 to 90.5 gm. There was complete healing of lesions. Patients with neurosyphilis showed marked improvement.

Treatment of early syphilis with penicillin and bismuth subsalicylate. Daily injection of 500,000 units of penicillin G in sodium chloride solution for twenty consecutive days and ten to twenty doses of bismuth subsalicylate at the rate of two a week. V. Pardo-Castello and Osvaldo A. Pardo. Arch. Dermat. & Syph., 61: 196–209, Feb. 1950.

AM. J. SYPH., GONOR. & VEN. DIS.—Con.

Of 41 patients treated at University of Havana Hospital and followed for 3 to 15 months, 26 achieved serologic reversal, while 15, still under observation, have falling titer. No clinical or serologic relapses occurred. There was no difference between the group that received 10 doses of bismuth and that which received 20 doses.

Viruses of special interest to the dermatologist. A review. M. R. Hilleman.
 Arch. Dermat. & Syph., 61: 210–236, Feb. 1950.

Among the viruses reviewed are those of the lymphogranuloma venereum group. Complement-fixation test is used to determine the diagnosis.

Tryparsamide and bismuth subsalicylate in the treatment of experimental syphilis of rabbits. Synergistic or additive activity. John A. Kolmer. Arch. Dermat. & Syph., 61: 271–275, Feb. 1950.

Single minimal curative dose of bismuth subsalicylate in oil in intramuscular injections was 0.008 gm. per kilogram of weight. Intravenous injection of tryparsamide in single dose of 0.05 gm. per kilogram was without synergistic or additive activity when administered with single intramuscular injections of bismuth subsalicylate, but showed some degree of activity when administered along with multiple doses of bismuth subsalicylate.

Reevaluation of Weltmann serum coagulation reaction in syphilis and various dermatoses. Louis Goldstein. Arch. Dermat. & Syph., 61: 285–296, Feb. 1950.

Technic of the Weltmann serum coagulation reaction is given in detail. Tendency toward widened coagulation bands was present in all stages of syphilis in direct proportion to the duration of the disease.

ARCH. OPHTH., CHICAGO

Differential diagnosis of pareses of superior oblique and superior rectus muscles. Peter J. Giotta. Arch. Ophth., 43: 1-8, Jan. 1950.

A discussion of differential diagnosis in cases of vertical muscle imbalance with head tilt and full binocular vision. Six illustrative cases are presented.

ARCH. PATH., CHICAGO

Acute esophagitis in infants. Peter Gruenwald and Memoir R. Marsh. Arch. Path., 49: 1-2, Jan. 1950.

A review is presented with syphilis being listed as one of the causes.

BULL ACAD. MED. CLEVELAND, CLEVELAND
The undiscovered. City-wide venereal disease educational program and case finding project. G. A. DeOreo. Bull. Acad. Med. Cleveland, 34: 8, 21, Sept. 1949.

In spite of the decrease in reported cases of gonorrhea and syphilis, reinfections are more common and congenital syphilis has shown no reduction. Therefore, Cleveland planned a drive for October and November of 1949.

BULL. GEORGETOWN UNIV. M. CENTER, WASHINGTON

Syphilitic aneurysm of the abdominal aorta with rupture into the stomach. Albert J. Finestone. Bull. Georgetown Univ. M. Center, 3: 123-127, Oct.-Nov. 1949.

A case is presented with a consideration of the possibility of erosion from the stomach into the aneurysm. The importance of establishing this difficult antemortem diagnosis is stressed because of newer surgical approaches to this problem.

Reactions to aureomycin. Frank J. Eichenlaub and Matthew A. Olivo. Bull. Georgetown Univ. M. Center, 3: 152, Dec. 1949–Jan. 1950.

A report is presented of a patient who developed herpes zoster and generalized papular eruption during administration of aureomycin by mouth, the reaction being considered a toxić reaction to the drug.

BULL. VEN. DIS., BOSTON

Gonorrhea. Lewis W. Kane. Bull. Ven. Dis., 13: 1-6, Jan. 1950.

Gonorrhea is discussed as to etiology, transmission, and incubation period, symptoms and signs, treatment, and public health aspects.

BULL. WORLD HEALTH ORGAN, GENEVA

Observations on the serodiagnosis of syphilis. J. F. Mahoney and Margaret R. Zwally. Bull. World Health Organ., 2: 227-231, 1949.

Biologic false-positive reactions and improvement in antigen composition are discussed. BULL. WORLD HEALTH ORGAN.—Continued

Rapid treatment of syphilis with penicillin. I. A survey of the problem. E. W. Thomas. Bull. World Health Organ., 2: 233-248, 1949.

Penicillin is discussed as to preparations, difficulties in evaluating therapy, serologic tests, and results of therapy in early and late syphilis.

Rapid treatment of syphilis with penicillin. Penicillin in prenatal and infantile syphilis. E. W. Thomas. Bull. World Health Organ., 2: 249-255, 1949.

Treatment during pregnancy with emphasis on requirements of ideal treatment and problems of penicillin treatment of infantile congenital syphilis are discussed.

Medical aspects of the causes and prevention of crime and the treatment of offenders. Manfred S. Guttmacher. Bull. World Health Organ., 2: 279-288, 1949.

In discussing causes of crime, it is pointed out that syphilis does not produce a weakening of the germ plasm, manifesting itself by criminalism in the progeny.

CANAD. J. PUB. HEALTH, TORONTO

Nomenclature and interpretation of results of serological tests for syphilis. E. L. Barton and W. Gordon Brown. Canad. J. Pub. Health, 40: 466-468, Nov. 1949.

Serologic findings presently reported negative, positive, and doubtful will be changed to—no reaction, reaction present, and inconclusive. Quantitative tests will be reported as the greatest dilution showing a reaction.

CANAD. M. A. J., MONTREAL

Modern treatment of neurosyphilis. George B. Sexton. Canad. M. A. J., 62: 43-47, Jan. 1950.

The treatment stressed is penicillin plus fever.

CHICAGO M. Soc. Bull., Chicago

The decade of the '40's—a review. Report-Division of Communicable Diseases, Illinois Department of Health. Chicago M. Soc. Bull., 52: 605-606, Jan. 21, 1950.

Incidence figures for 1949 are given for various diseases, including gonorrhea and syphilis, and compared with figures for 9-year median (1940–48). Gonorrhea cases, though but a fraction of 1 percent above reports in 1948, were 28 percent above 9-year median. Syphilis cases declined by 18 percent over 1948 and were 37 percent below 9-year median.

CHRIST HOSP. M. BULL., CINCINNATI

Cardiovascular syphilis. George X. Schwemlein. Christ Hosp. M. Bull., 3: 27-29, Oct. 1949.

Adequate treatment of early syphilis prevents cardiovascular syphilis; however, therapeutic success lies largely in recognition of aortic involvement before the development of valvular insufficiency or saccular aneurysm.

GASTROENTEROLOGY, BALTIMORE

A new diagnostic criterion for gastric syphilis. Herbert Berger. Gastroenterology. 14: 147-151, Jan. 1950.

This paper is presented primarily to reawaken interest in gastric syphilis. In addition to other criteria, rapid antisyphilitic therapy with penicillin makes it easier to fulfill that of symptomatic relief and/or disappearance of roentgen defect.

HEALTH, TORONTO

National Social Hygiene Day, Feb. 1, 1950. Editorial. Health, p. 5, Jan.-Feb. 1950.

Social hygiene goes far beyond the problem of mere treatment—its theme for the day "conduct and not medication is the true prevention of venereal disease."

Is syphilis vanishing? D. R. S. Howell. Modern Trends. Health, p. 31, Jan.-Feb. 1950.

Clinics are noting a great decrease in the number of new cases. Chicago is cited' as an example, cases dropping from 200 per week to 10 per week. It seems that penicillin has diminished its infectivity.

J. A. M. A., CHICAGO

Prophylactic administration of penicillin to obstetric patients. William C. Keettel and E. D. Plass. J. A. M. A., 142; 324-328, Feb. 4, 1950.

In a study of pregnant women in Iowa University Hospital, penicillin was effective in reducing puerperal morbidity, but in treatment of ophthalmia neonatorum it was no more effective than silver nitrate.

Antitreponemal effect of chloramphenicol. J. A. M. A., 142: 422, Feb. 11, 1950.

Chloramphenicol administered in total

J. A. M. A.—Continued

daily dosages of 120 mg., 60 mg., or 30 mg. per kilogram of body weight for a 6-, 4-, or 8-day period produced healing of lesions of early syphilis. Procedure not recommended for other than experimental purposes.

J. AM. M. WOMEN'S A., NASHVILLE

The treatment of syphilis. Katherine H. MacEachern. J. Am. M. Women's A., 5: 69-72, Feb. 1950.

A review of the literature and accepted treatment schedules for various manifestations of syphilis are given. Penicillin G is said to be the most effective antisyphilitic drug thus far discovered.

J. FLORIDA M. A., JACKSONVILLE

Reliability of serologic examinations as performed in medical laboratories in Florida. Albert V. Hardy. J. Florida M. A., 36: 427-429, Jan. 1950.

With each of three series of blood specimens distributed by the Venereal Disease Research Laboratory to evaluate syphilis serology in several Florida laboratories, progressive improvement in results was noted. In the last series, two-thirds of findings were excellent.

J. INVEST. DERMAT., BALTIMORE

A comparison of the cup-plate and serial dilution methods of penicillin assays. D. K. Kitchen, E. W. Thomas, C. R. Rein, and W. E. Crutchfield, Jr. Preliminary and Short Reports. J. Invest. Dermat., 14:5-7, Jan. 1950.

Both assay methods were performed simultaneously in checking amount of crystalline sodium penicillin G in known standards prepared in gelatin, phosphate buffer, and human serum diluents. Under conditions studied, cup-plate assay procedure was more accurate than serial dilution method.

J. M. A. GEORGIA, ATLANTA

The prevention of congenital syphilis. Rudolph W. Jones, Jr. Georgia Department of Public Health. J. M. A. Georgia, 39: 38-39, Jan. 1950.

Prevention can be effected by: obtaining serologic tests on every woman at the initial prenatal visit and during the last trimester, instituting penicillin therapy if in doubt as to activity of a syphilitic infection, and performing repeated serologic tests on infants born of syphilitic parents for 6 months after delivery.

J. Mt. SINAI HOSP., NEW YORK

Production of a constant plasma penicillin level by means of daily injections of procaine penicillin in oil with aluminum monostearate. Louis E. Schaefer and Ira A. Rashkoff. J. Mt. Sinai Hosp., 16: 300-302, Jan.-Feb. 1950.

Average therapeutic plasma penicillin level of 0.5 units per cubic centimeter was maintained in 19 patients after the fifth injection of 300,000 units of procaine penicillin in oil with aluminum monostearate.

J. NAT. M. A., NEW YORK

The diagnosis of congenital syphilis in early infancy. Armen G. Evans. J. Nat. M. A., 42: 8-10, Jan. 1950.

Diagnostic factors such as rhinitis, cutaneous lesions of various types, and a diffuse eruption which gives the skin a copper-like appearance are discussed.

J. SOCIAL HYG., NEW YORK

International VD activities of the U.S. Public Health Service. Theodore J. Bauer. J. Social Hyg., 36: 35-36, Jan. 1950.

The Office of International Health Relations advises the State Department on matters relating to WHO and arranges American representation at all international health conferences.

The communities vs. the prostitution racket. Paul M. Kinsie. J. Social Hyg., 36: 45, Jan. 1950.

An account of how Charleston, S. C., overcame the menace of prostitution is presented.

The function of the police in yenereal disease control. John A. Chisholm. J. Social Hyg., 36: 53-56, Feb. 1950.

A-review of steps which police can take to suppress prostitution and promiscuity is presented.

Cooperation in VD control. Charles A. Higgins. J. Social Hyg., 36: 61-64, Feb. 1950.

The Rhode Island educational casefinding campaign against syphilis, enlisting cooperation of the Armed Forces Disciplinary Control Board and the Providence Board of Health, is discussed.

J. SOUTH CAROLINA M. A., FLORENCE

Outline of treatment S. C. Health Hospital, Florence, South Carolina, November 1, 1949. Public Health News. J. South Carolina M. A., 46: 31, Jan. 1950.

Treatment schedules are outlined for various stages of syphilis and for chancroid, lymphogranuloma venereum, and granuloma inguinale.

LANCET, LONDON

Syphilitic bursitis with report of a case.
E. W. Prosser Thomas and A. J. Rook.
Lancet, 2: 1221-1222, Dec. 31, 1949.

Case reported is one of 64-year-old woman who complained of pain and swelling of knee. Lesion healed satisfactorily with bismuth and penicillin treatment.

M. TECHNICIANS BULL., WASHINGTON

BuMed circular letter no. 49-116. Sept. 23, 1949. M. Technicians Bull., 1: 25-28, Jan.-Feb. 1950.

Subject is treatment of syphilis and gonorrhea as recommended for Navy personnel.

M. WORLD, LONDON

Treatment before diagnosis. L. W. Harrison. M. World, 71: 511-516, Dec. 9, 1949.

This is a discussion on the question, "Is treatment before diagnosis on suspicion of venereal disease advantageous to (a) the patient, (b) public health?"

NEW ORLEANS M. & S. J., NEW ORLEANS

Pathology of certain inflammatory lesions and neoplasms of the small bowel. William H. Harris. New Orleans M. & S. J., 102: 340-347, Jan. 1950.

Congenital syphilis is given as one cause of intestinal involvement. Intestinal lesions are rare in acquired syphilis.

Conservative management of chronic cervicitis.
Oran V. Prejean.
New Orleans
M. & S. J., 102: 365-370, Jan. 1950.

In discussing etiology, the author states that the chronic infective organism is usually a streptococcus with its invasion made possible by other organisms such as *Neisseria gonorrhoeae*.

SOUTH. M. J., BIRMINGHAM

The effectiveness of Alabama's mass blood testing program. W. H. Y. Smith and D. G. Gill. South. M. J., 43: 185-190, Mar. 1950.

Rate of syphilitic infection for 449,373 white males tested was 1.17 percent; 508,049 white females, 1.32 percent; 214,835 Negro males, 15.14 percent; 261,978 Negro females, 18.78 percent. The Negro rate was 14 times the rate for the white man.

Recent advances in antibiotic therapy with special reference to aureomycin and chloramphenicol. Harry F. Dowling and Mark H. Lepper. South. M. J., 43: 190-195, Mar. 1950.

Lymphogranuloma venereum has responded dramatically to aureomycin. Good results have also been observed in granuloma inguinale.

Tr. & Stud., Coll. Physicians, Philadelphia, Philadelphia

Comparison of oral penicillins. William P. Boger, John O. Beatty, and Harrison F. Flippin. Tr. & Stud., Coll. Physicians, Philadelphia, 17: 105-114, Dec. 1949.

From a study at the Philadelphia General Hospital and University of Pennsylvania Hospital, it was shown that five oral penicillins and intramuscular penicillin, when compared at a level dosage of 200,000 units, resulted in urinary recovery over a 3½-hour period of one-sixth as much after oral as after intramuscular It was further shown administration. that the plasma concentrations after intramuscular penicillin varied in their relationship to those after oral administration from as much as 35 to 1 at ½ hour, to a ratio of 1:1 at 31/2 hours after administration of antibiotic.

UNIV. HOSP. BULL., ANN ARBOR

Differences in specificity of cardiolipin and Kahn antigens in 1949 National Serologic Evaluation Survey. Elizabeth B. McDermott and Reuben L. Kahn. Univ. Hosp. Bull., 15: 93-94, Nov. 1949.

The 1949 study, performed at Venereal Disease Research Laboratory, Staten Island, N. Y., was based on examination of 386 blood specimens, of which 237 were from syphilitic and 149 from normal nonsyphilitic donors. The study revealed that the incidence of false-positive reactions reported by various State public health laboratories and control laboratories was far greater with tests employing cardiolipin antigen than with the Kahn test employing Kahn antigen.

STATISTICS

Cases of Venereal Disease Reported to the Public Health Service by State and Territorial Health Departments, Fiscal Year 1949 (By Disease, Stage and Reporting Source)

[Known military eases exeluded]

Lymphogranu- loma vene- reum		Other	111 0 0 0 0 0	245 5 6 197 197 37	394 104 47 36 134 108	90 3 31	182 172 170 9 0
Lymphe	loma vene-	Pri- vate physi- eian	000000	EI 0 4 6 6 0	000000	000-7	00 17 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	nale	Other	000000	176 1 7 108 108 60	323 63 106 47 76 4	42 21 19	62 49 49 13 0
Granuloma inguinale		Pri- vate physi- eian	00000	10 10 00 0	0010017	4088	₩. T 4 0 0
	eroid	Other a	26 0 18 0 0	516 4 8 431 428 73	1, 434 709 155 133 315 100	538 424 90	290 245 245 26 0 0
Chaneroid		Pri- vate physi- eian	11 22 10 00	29 0 11 16 0 0	2044×200	36	25 14 20 00 20
	Gonorrhea	Other a	2, 657 523 144 1, 823 158 0	35, 245 145 3, 288 21, 372 19, 450 10, 440	48, 563 13, 255 6, 806 5, 562 14, 928 9, 748 3, 826	20, 973 5, 505 6, 530 8, 938	25, 291 21, 906 19, 368 2, 430 2, 485 470
Gono		Pri- vate physi- eian	1,840 431 195 697 128 153 236	7, 639 85 1, 524 6, 030 2, 981	6, 972 3, 434 677 395 433 1, 547 881	5, 687 582 2, 652 2, 453	6, 376 4, 935 1, 856 1, 479 576 386
	Stage not stated	Othera	135 73 5 0 0 0 56 1	438 72 115 186 159 65	200 109 103 0 90 0	183 7 176 0	400040
		Pri- vate physi- eian	334 92 92 0 0 4 1111 122	338 91 25 143 104 79	63 27.2 0 0 0	969 43 926 0	041000
	Congenital	Othera	101 112 122 722 0 0	968 14 126 372 324 456	1, 055 92 255 153 368 170 170	659 1115 196 348	262 262 188 230 230 23
		Pri- vate physi- eian	166 34 14 11 29 23	511 12 96 357 214 46	156 16 16 16 36 36	721 62 220 439	488 212 213 68 162 23 91
	Late and late latent	Other	1, 130 77 72 721 150 0	13, 977 11, 919 8, 338 7, 045 3, 601	7, 362 1, 384 2, 717 2, 112 1, 016 1, 231 1, 014	6,317 900 2,254 3,163	4, 410 2, 970 2, 151 294 163
ilis		Pri- vate physi- eian	1,371 266 116 528 100 315 46	12, 113 83 2, 463 8, 603 5, 898 964	2, 511 143 442 276 213 648 1, 065	10, 498 1, 100 2, 568 6, 830	7, 081 4, 262 1, 779 1, 337 1, 103
Syphilis	latent	Other a	366 103 46 175 2 40 0	9, 067 175 1, 553 3, 277 3, 126 4, 062	7, 696 1, 779 1, 130 2, 654 1, 657 614	4, 547 690 1, 367 2, 490	3, 572 2, 623 2, 088 761 63 125
	Early latent	Pri. vate physi- eian	432 141 51 122 28 79 11	4, 216 160 1, 309 2, 175 1, 923 572	2,300 127 206 130 307 910 750	5, 196 573 741 3, 882	2,976 1,893 1,129 675 94 314
	Primary and secondary	Other a	378 53 68 214 2 41 0	4, 577 78 530 2, 266 2, 007 1, 703	6, 267 814 1, 427 2, 279 1, 131 616	2, 858 713 888 1, 257	2, 479 1, 787 1, 322 1, 572 31 89
		Pri- vate physi- eian	710 107 196 235 69 69 43	2, 241 95 471 1, 454 1, 023 221	1, 498 44 269 135 139 461 585	2,332 377 758 1,197	2, 161 1, 328 1, 328 633 531 92 210
	Total	Other a	2, 110 415 208 1, 182 11 293 1	29, 027 458 4, 243 14, 439 12, 661 9, 887	22, 580 3, 283 6, 287 4, 385 6, 317 4, 279 2, 414	14, 564 2, 425 4, 881 7, 258	10, 994 7, 642 5, 749 2, 546 400
		Private physi- eian	3, 013 640 382 940 212 577	19, 419 441 4, 364 12, 732 9, 162 1, 882	6, 528 323 960 569 675 2, 085 2, 485	19, 716 2, 155 5, 213 12, 348	12,715 7,695 3,609 2,707 1,718
Federal Sceurity Agency regions		Region 1—Total Connecticut. Maine. Massehusetts. New Hampshire. Rhode Island.	begion 2—Total	District of Columbia. District of Columbia. Maryland. North Carolina. North Carolina. Virginia.	Region 4—Total Kentucky Wiehigan	Region 5—Total. Illinois. Officago	

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80, 621 14, 001 15, 324 8, 826 9, 231 19, 728 9, 101	7, 190 1, 125 4, 815 3, 157 622 0	36, 084 3, 478 12, 250 869 5, 396 14, 091	2, 173 1, 429 309 154 228 53	24, 721 819 20, 493 354 735 2, 117 203	653	274, 095	284, 171
7,419 1,621 1,764 1,764 1,190 2,799 2,799	2,330 630 310 742 311 274 311 186 188	13, 357 1, 326 170 170 148 765 10, 948	610 268 80 85 91 86	6, 496 132 4, 267 282 273 421 565 565	0	57, 600	58, 726
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2, 784 2, 784 0 0 0 0 16 0 0	467 0 0 199 0 199 23 23	6,008 46 756 0 112 5,094	24 0 62 4 0 51	207 777 0 0 0 477 76	0	11,154	11, 237
4, 676 414 470 1, 116 256 217 1, 272 15	262 19 76 141 54 54 0	3, 645 1, 135 1, 135 676 93 164 1, 577	255 16 16 6 8 8 6	389 389 151 10 10 10 86 86 89 89 89	2.0	11, 194	12, 522
208 1255 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	307 101 104 22 22 7	233 100 11 23 84 15	32 32 14 22 52	280 10 189 20 20 11 11 25 25	0	3, 101	3, 145
17, 751 2, 748 3, 318 5, 878 1, 198 1, 398 1, 398	2,588 251 699 1,471 781 114 0 53	13, 922 5, 850 3, 344 387 1, 023 3, 318	463 212 110 25 26 29 86	6, 672 341 5, 261 152 236 552 0	125	73, 012	74, 717
2, 486 2, 486 103 385 146 950 0	3,502 1,050 1,327 773 379 79 51	2, 714 1, 146 1, 146 81 112 1, 096 279	755 293 26 193 174 69	4, 031 3, 050 3, 050 1122 236 107	0	48, 921	49, 175
21, 236 3, 050 3, 026 3, 452 3, 452 3, 716 1, 478 3, 380	1,718 149 315 1,065 623 89 0 0	10, 902 2, 194 2, 938 414 638 4, 718	291 120 41 61 61 54	3,444 2,511 2,511 142 329 0 388	72	59, 370	62, 911
2, 276 2, 276 340 108 828 0	1,855 292 371 887 497 186 54 65	1, 991. 1, 035 33 101 572 250	361 165 17 77 36 66	1, 573 1, 226 1, 226 45 73 92 30	0	24, 972	25, 094
11, 669 1, 900 1, 964 2, 546 1, 874 1, 479 1, 326 2, 556	1, 124 121 195 671 329 58 0 0	5, 951 799 1, 721 170 687 2, 574	258 142 43 43 34 30 9	2, 573 325 1, 793 1, 793 141 259 0	56	37, 544	38, 160
3,317 1,296 1,296 474 354 372 326 0	1, 509 295 299 639 217 123 90 63	1, 237 445 29 58 197 508	334 146 146 17 77 57 40	1, 440 59 1, 101 74 93 46 9	0	16, 724	16, 779
55, 640 8, 586. 8, 586. 10, 499 11, 751 5, 649 4, 141 6, 646 159	5,778 540 1,310 3,396 1,787 1,285 0	35, 289 9, 990 9, 495 1, 064 2, 553 12, 187	1, 113 499 225 129 208 528	13, 824 1, 112 10, 500 232 529 1, 234 217	235	183, 897	191, 154
15,118 4,452 6,183 600 1,104 629 2,150 0	7, 640 1, 267 1, 861 3, 156 1, 513 253 194	12, 183 2, 772 910 2, 061 6, 146	1, 567 636 82 365 289 195	7,531 167 5,643 456 247 460 340 218	0	104, 872 183, 897	105, 430
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Clinics, hospitals and other institutions.

Canal Zone.....

Oregon Washington

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Region 10-Total... Arizona

California____

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Montana Utah Wyoming

June 1950

Source: PHS Form 8958-B FSA-PHS—Division of Venereal Disease, Office of Statistics, 3/24/50 (ML-MC) nw.

Region 9-Total.

Texas....

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Region 8—Total.....

Venereal Disease Information,

Arkansas.... New Mexico...

Louisiana....

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Region 6—Total

Florida_____ Georgia...... Mississippi...... South Carolina.....

The Journal of

Tennessee______Virgin Islands______

Region 7-Total..

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DOCUMENTS SECTION

The JOURNAL of VENEREAL DISEASE INFORMATION

July 1950 Volume 31 Number 7 Congenital Syphilis Issue **EDITORIAL Teamwork** 173 ORIGINAL ARTICLES A Proposal for Joint Action Against Congenital Syphilis . . 174 BETTY HUSE, M. D. W. H. AUFRANC, M. D. Status of Treatment of Syphilitic Pregnant Women and of Children Who Have Congenital Syphilis 178 MARY S. GOODWIN, M. D. How To Evaluate Positive Kahn Tests in Infants . 185 HERMAN N. BUNDESEN, M. D. HANS C. S. ARON, M. D. The Dentist's Role in Finding Congenital Syphilis 191 FRANK P. BERTRAM, D. D. S., M. P. H. CURRENT NOTES AND REPORTS . . 193 CURRENT LITERATURE 194 STATISTICS Reported Cases of Civilian Congenital Syphilis, Fiscal Years 1940-50, by Quarters 197



FEDERAL SECURITY AGENCY Public Health Service

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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PUBLIC HEALTH SERVICE

LEONARD A. SCHEELE, Surgeon General

Editor: THEODORE J. BAUER, Medical Director Chief, Division of Venereal Disease

The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

Editorial

Teamwork

When the Association of State and Territorial Health Officers met with the Public Health Service and the Children's Bureau last October, I stressed the need for teamwork among all groups concerned with the peoples' health. I was especially impressed, therefore, by the Association's recommendation that the maternal and child health and the venereal disease control staffs of State health departments unite in joint planning and in action for the prevention of congenital syphilis.

The proposal by Dr. Huse and Dr. Aufranc, published in this issue of The Journal of Venereal Disease Information and simultaneously in *The Child*, represents the same kind of teamwork between the Children's Bureau and the Public Health Service, in an effort to solve a common problem. Miss Lenroot and I heartily endorse their suggestions for joint action in State and local agencies.

For the past 5½ years, the incidence of congenital syphilis has been reported as remaining constant, in spite of consistent declines that have occurred in morbidity reporting of primary and secondary syphilis. Cooperative action by venereal disease control and maternal and child health programs for the prevention of congenital syphilis would give thousands of infants a better chance for life and health.

We need not wait for further developments in the field of medicine in order to prevent congenital syphilis. We have effective diagnostic technics. We know that in most cases penicillin administered during pregnancy to women infected with syphilis will insure the birth of a nonsyphilitic child.

Congenital syphilis control comes within the scope of many medical and social services, public and private. Physicians in general practice, obstetricians, and pediatricians—all of whom provide such a large share of prenatal and infant care—are indispensable allies of public health groups aggressively attacking congenital syphilis. Visiting nurse associations, hospitals, clinics, family service agencies, midwives, and other community groups have close relationships with mothers and children. All these groups are members of the team which will work together to find and treat syphilis in pregnant women and in children.

Congenital syphilis is preventable. We have the medical means to eliminate it. To do so, we must make every effort to find the syphilitic pregnant woman and treat her. Teamwork is the key to accomplishing that task.

Leonard A. Scheele, Surgeon General.

A Proposal for Joint Action Against Congenital Syphilis

Betty Huse, M. D., and W. H. Aufranc, M. D.

When a child has been infected with syphilis by his mother before he is born, we call his disease congenital syphilis. A better name would be "negligent" syphilis, because, as doctors have pointed out repeatedly, negligence is the only reason today for any child in the United States to be born with syphilis.

Yet some 100,000 children in this country 10 years of age or less are estimated to have undiscovered congenital syphilis. Any one of these children is a candidate for blindness, mental deficiency, physical deformity, or premature death. Not one of them should have been born with syphilis.

For the past 4 years penicillin has been widely available, and effective for the treatment of syphilis. Nevertheless, about a third of the 14,000 cases of congenital syphilis reported each year are children 4 years old or younger.

The venereal disease program is concerned with eliminating syphilis from the population. The maternal and child health program is concerned with the health of mothers and children. When babies are infected during their mothers' pregnancy, the mandate for joint action is unmistakable.

We therefore propose joint action by the venereal disease and maternal and child health programs—to find and treat every syphilitic pregnant woman and to find and treat every syphilitic newborn baby.

As a basis for joint action, the Public Health Service and the Children's Bureau have agreed upon certain basic procedures:

- 1. We recommend that at least two blood tests for syphilis be made as a routine part of every woman's prenatal care—one early in pregnancy, the other late in the third trimester or at the time of delivery. This recommendation is of sufficient importance to merit consideration for legislative action.
- 2. Since a pregnant woman with untreated syphilis is a medical emergency, we recommend that she receive treatment at once.
- 3. If a mother has received no prenatal care prior to delivery in a hospital, we recommend that a blood test for syphilis be made at the time of her admission. If the test is positive, the mother should be treated. Treatment of the mother, even when given immediately before delivery, offers some protection to the baby.
- 4. For all babies born of untreated or inadequately treated syphilitic mothers, we recommend that a blood test for syphilis be made as soon as possible. new filter paper microscopic (FPM) test (1) promises to be satisfactory and to eliminate the difficulty of obtaining venous blood from a baby.) A positive test of the infant's blood may not indicate the presence of syphilis; similarly, a negative test may not indicate the absence of syphilis. If the chances are not good that the physician will be able to observe the infant over a minimum period of 4 months, he may wish to give protective penicillin therapy. If the physician elects to delay treatment, it will be on the assumption that his chances for observing the child for a minimum period of 4 months are very good indeed. If signs of syphilis do not appear within the first 4 months and if the blood test is negative at that time, it is extremely unlikely that evidence of congenital syphilis will appear later.
- 5. Even if the mother has been treated for syphilis, either before pregnancy or early in pregnancy, we recommend that the infant's blood be tested for syphilis

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Note: This article is being published simultaneously in the June-July issue of *The Child* (monthly bulletin issued by the Children's Bureau).

at birth. If the test is positive, even though this does not necessarily indicate congenital syphilis, the doctor's decision to give protective penicillin therapy should depend, as before, on whether or not he will be able to observe the baby for at least 4 months. If the test is negative and if the mother's syphilitic status is quiescent, there is little or no likelihood that congenital syphilis will develop.

We have recommended that every pregnant woman be given at least two blood tests for syphilis as a routine part of her prenatal care. If this recommendation is to be carried out successfully, we must enlist the pregnant woman herself as a partner. She must be encouraged to request blood tests for syphilis as a routine part of her prenatal care. Maternal and child health services throughout the country are in a position to reach a large reading and listening audience of pregnant women. The venereal disease public appeal program can reach an equally large audience.

The workers in venereal disease control should plan to broaden their emphasis in epidemiology and case finding so as to include not only contact interviewing and contact tracing on primary and secondary syphilis but also to make certain that examinations for syphilis are performed on all children of syphilitic mothers and on all brothers and sisters, as well as parents, of children with congenital syphilis to insure that no case of congenital syphilis goes undiscovered and that other cases of congenital syphilis do not occur.

We should also enlist the general practitioner and the obstetrician in our search, All State maternal and child health programs maintain continuing relationships with these physicians. Many of the State medical societies have a maternal and child health committee, with which the maternal and child health division of the State health department works very closely. (This collaboration has made possible many studies of maternal deaths, the findings of which have been of material assistance in reducing maternal mortality in this country.) Here is an established mechanism that can be put to good use in the field of congenital syphilis. Where the medical society has both a venereal disease committee and a maternal and child health committee, they might work together.

Perhaps some combination of the two committees and the two divisions could study each reported case of congenital syphilis, going back to the prenatal history to find out just why the disease had not been prevented. Such a study would shed light on the specific measures that should be taken in the State to tighten up case finding and treatment among pregnant women.

Through refresher courses, institutes, seminars, talks before medical societies, and publications, professional education can be provided for doctors, nurses, medical social workers, nutritionists, and others who come in contact with pregnant women.

Many pregnant women are cared for, if at all, by midwives. In 1947, midwives delivered about 176,000 babies in the United States, most of them in southern and southwestern States. In many of these States the maternal and child health division of the health department is concerned with trying to raise the standards of midwife care. Where there is a State law concerning midwives, licensing and regulatory powers frequently are vested in the maternal and child health division of the health department. We are not very hopeful of raising the midwife standards dramatically, but it has been possible through law, regulation, or persuasion to get some of these maternity patients to a doctor for at least one examination. Added effort might cause this to happen more often, and the doctor giving the examination could be persuaded to test the woman for syphilis the first time he sees her and again late in the third trimester.

In some States welfare funds are made available for the medical care of welfare clients, including pregnant women. The child welfare division of the welfare department, in some States, takes considerable responsibility for the care of unmarried pregnant women, including the arrangements for their medical care. The maternal and child health division of the health department can alert the various welfare departments to the necessity for testing pregnant women at least twice.

Many health department clinics are satisfied with *one* blood test during the prenatal period, and this may be responsible for some of the failures to prevent congenital syphilis. This situation should be corrected, since the woman may contract syphilis after the blood test is made.

We have recommended that since a syphilitic pregnant woman is a medical emergency she should receive treatment at once. The physician should report the case immediately to the health department, and treatment should be started without delay. Many of these patients can be treated in rapid treatment centers or in beds contracted for in hospitals. Perhaps even more could be treated in these centers if the maternal and child health division were to help out with delivery facilities, obstetrical consultation, and the satisfactory care of the well children who must sometimes accompany their mothers to the centers. The maternal and child health program frequently has consultants on pediatrics, obstetrics, nursing, medical social services, and nutrition. They can be called upon to help.

It is frequently difficult or even impossible for a woman in the last trimester of pregnancy to leave home long enough for rapid treatment at one of the centers. In such cases the maternal and child health service might help to arrange for treatment in a prenatal clinic, hospital clinic, or doctor's office.

We have recommended that if a mother has received no prenatal care prior to delivery a blood test for syphilis be given her at the time of her admission to the hospital. To make this testing effective as an instrument in our search, the rapid processing of blood tests on this group of patients is essential. This can and should be done. Rapid processing is especially important in these days of short mater-

nity stays. Since the maternal and child health program is concerned with hospital facilities and with the standards and procedures related to maternity care, it should be helpful in promoting this testing in hospitals. Most State programs have an active hospital consultation service. Their relationships with the obstetric and pediatric staffs have been influential in improving hospital practices for the care of mothers and children.

We have recommended that babies' blood should be tested at birth if they are born of syphilitic mothers who have not been treated or who have been treated before pregnancy or early in pregnancy. Success in accomplishing this, as well as in assuring appropriate treatment and follow-up, depends primarily on the understanding of physicians—general practitioners, obstetricians, and pediatricians—and on hospital policies. Here again, the maternal and child health program can help through its relationships with hospitals and with doctors who are taking care of mothers and children.

But what of the children of syphilitic mothers who, by some chance, have not been blood-tested or treated in the neonatal period? Case finding among babies and preschool children has presented many difficulties, not the least of which has been that of obtaining blood from a But with the filter paper microscopic test or some similar one it should be much easier to find these children in the future. The maternal and child health service should be able to find cases through the well-child clinics and through the physicians and clinics that provide health supervision to babies and young children.

The question is frequently raised as to whether a routine blood test should be made on all school children. This would probably not be worth while if attempted on a national scale. However, in some areas of relatively high prevalence of syphilis, mass testing of children under 15 years of age has found roughly 3 to 13 percent positive or doubtful reactions among Negro children and about 1 to 4 percent among white children. In one

such area about 2 percent of the blood tests given to Negro children resulted in finding previously untreated syphilis and, in another area, 4 percent. These data would seem to warrant mass blood testing on school children in areas of high prevalence. It would be desirable and practical if such blood testing were part of a more inclusive health screening procedure that would include tests for visual and hearing defects, anemia, and other physical handicaps.

School health services of some kind are provided in almost half the counties of the United States. Whether these services are the responsibility of health or of education authorities, the maternal and child health division of the health department is in a position to exert considerable influence on screening procedures for children of school age.

Summarizing briefly—

In almost any State the maternal and child health program and the venereal disease control program can assist each other in this joint program against congenital syphilis.

The investigation of sex contacts and of family contacts and the presentation to the general public of the facts involved would be handled best within the venereal disease control program.

The maternal and child health program is in a position to pass the word along to mothers, to professional workers, and to hospitals and other agencies that care for mothers; to encourage blood testing as a routine part of prenatal care; to exert a certain amount of influence on hospitals; to work with midwives; and to work with school health services.

Both programs can extend the message to specific population groups. Both can reach a large percentage of parents directly through bulletins and pamphlets and through parent-teacher associations and other parent groups.

Both the Children's Bureau and the Division of Venereal Disease of the Public Health Service are willing to devote every available channel of communication to telling the public or groups within the population the story of congenital syphilis.

To us a child with congenital syphilis is a child with a general disease—a child who is likely to need special help to achieve optimum physical and emotional health even when his syphilis is cured. We suggest, therefore, that venereal disease personnel call on the maternal and child health services for assistance in obtaining the pediatric and auxiliary services—nursing, medical social, and nutritional—that these children may need.

This statement is quite frankly a plea for mutual assistance and action in the control of congenital syphilis rather than a blueprint for action. We do not know precisely what form this assistance might take in the various States; but we are convinced that, if Federal, State, and local programs merge both venereal disease control and maternal and child health activities into a single program for immediate action in controlling congenital syphilis, there will be a sharp downward trend in congenital syphilis in the not too distant future.

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Status of Treatment of Syphilitic Pregnant Women and of Children Who Have Congenital Syphilis¹

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Treatment of Pregnant Women

An ideal plan of antisyphilitic therapy for pregnant women has been outlined (1) as one which offers freedom from serious toxic effects, adequate therapy in a short period of time, cure of the maternal syphilis, prevention of the transmission of the disease from mother to baby, and cure of the congenitally syphilitic child in utero when infection may already have been transmitted. Extensive clinical data, reported in a voluminous literature, has demonstrated that penicillin fulfills these requirements better than any other drug or combination of drugs available.

Adequate therapy of the infected mother with penicillin is nearly 100-percent effective in preventing the congenital form of Reports of more than 850 the disease. syphilitic pregnant women treated with various types of penicillin and with several different dosage schedules were reviewed in the literature prior to January 1, 1950 (1–11). These pregnancies resulted in 15 living syphilitic infants, a failure rate of 2 percent, which contrasts very favorably with the expected failure rate of from 5 to 50 percent or more when metal chemotherapy is used, depending on the time in pregnancy of beginning such therapy, the amount administered, and the stage of the syphilitic infection in the mother.

Moreover, the failure rate with penicillin can be still further reduced, perhaps to zero, by adequate prenatal care of the mother so that (1) her infection may be recognized and treatment given before the fetus is infected and so that (2) re-treatment may be given to the patients who have failed to respond satisfactorily to the initial course of treatment and to those who develop an infectious relapse or a

reinfection late in pregnancy. To achieve a negligible failure rate, monthly prenatal examinations are essential for all women treated with penicillin. It is never too late to give the necessary treatment, and success has been reported even when it has been completed during labor (1).

Aqueous Penicillin

When aqueous penicillin is used for the treatment of syphilitic pregnant women, the minimum recommended dosage is a total of 2.4 million units administered in doses of 40,000 units every 3 hours for 60 intramuscular injections $(7\frac{1}{2} \text{ days}).$ Because there was some question as to whether this amount had a maximum curative effect on the maternal syphilis, larger doses have been recommended by several authors. Speiser (1), for example, suggested 4 million units, to be given in doscs of 40,000 units every 3 hours for 100 doses, but most of the recent reports (5, 12, 13, 14) indicate that the incidence of syphilitic outcomes is negligible providing the amount administered is at least 2.4 million units.

Use of Arsenic, Bismuth, and Mapharsen

There is general agreement that arsenic and bismuth add nothing to penicillin therapy during pregnancy and that they should not be used (3, 11, 14, 15). The possible additive activity of penicillin by oral administration with mapharsen and with bismuth is discussed by Kolmer (16) in a paper on rabbit syphilis, which raises interesting possibilities for further investigations. These remain in the purely hypothetical stage.

Penicillin in Peanut Oil and Beeswax (POB)

An obvious draw-back to the use of aqueous penicillin was the necessity for hospitalizing all patients needing treatment, but the introduction of delayed-

¹ Presented at the Venereal Disease Control Seminar, New York, N. Y., March 28-29, 1950.

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absorption preparations in 1946 opened the way towards a partial solution of this problem. In 1947, Ingraham and his coworkers reported a group of 45 pregnant women treated with penicillin in peanut oil and beeswax with fairly satisfactory results—a failure rate of 4.9 percent (7). They advised against its use in the latter part of pregnancy because of the erratic blood and tissue levels obtained with POB, but in situations in which hospitalization was out of the question and no other treatment available they suggested that patients be treated with 4.8 million units of POB, either with 600,000 units daily in single injections for at least 8 days or with 300,000 units daily for 16 days. The recommendation is still valid, though it was originally offered with the reservation that large-scale studies using the drug for the ambulatory treatment of pregnant women had not been made.

Procaine Penicillin in Oil

The introduction of procaine penicillin in oil was a further advance. Ingraham (17) recently reported 62 syphilitic pregnant patients treated with this preparation without a failure.

Penicillin With Aluminum Monostearate

When it was found that the addition of aluminum monostearate to mixtures of the insoluble salts of penicillin and oil still further delayed the absorption of the drug (18), an even more adequate preparation for ambulatory treatment became available. Single injections of 1.2 million to 2.4 million units of procaine penicillin

G in oil containing 2 percent of aluminum monostearate have given measurable blood concentrations of penicillin for at least 5 days and occasionally for as long as 7 days.

Preliminary clinical studies based on treatment with aluminum monostearate are not yet complete, but these new schedules appear to be as satisfactory as previous schedules (14). This suggests that it may soon become possible to shift the care of pregnant syphilitic women to a completely out-patient status. At the present time a possible schedule using monostearate consists of 1.2 million units once a week for from 2 to 4 weeks (a total of from 2.4 to 4.8 million units). Another possible schedule is 1.2 million units in a single injection.

Re-treatment of the Pregnant Woman

The question of the need for re-treatment in subsequent pregnancies of previously adequately treated syphilitic women seems at last to be answered (19, 20).

Mothers Initially Treated With Arsenicals

In 1948 the Family Clinic of the Johns Hopkins Hospital reported their observations of 363 syphilitic women originally treated with metal chemotherapy who were allowed to go through 570 subsequent pregnancies without re-treatment (table 1). The initial criteria for admission to the study included: (1) Prior to the deliberately untreated pregnancy, a reasonably accurate history of maternal

Table 1.—Summary of studies of previously treated syphilitic women who were not re-treated in subsequent pregnancies

Physician making study	Mothers	Pregnancics	Normal infants	Infants with congenital syphilis	Non- syphilitie disasters
Total studied	587	819	747	2	71
Treated initially with arsenic: Goodwin	363	570	523	0	48
Treated initially with penicillin Speiser Ingraham Tucker	224 84 52 88	249 86 52 111	224 81 46 97	$\begin{smallmatrix}2\\&&1\\&&0\\1\end{smallmatrix}$	23 4 6 13

infection of at least 2 years' duration, for which 2.0 to 4.0 gm. or more of arsphenamine plus concomitant bismuth or mercury had been received; (2) negative maternal blood serologic tests before and during the current pregnancy; (3) normal maternal spinal fluid test; (4) no clinical evidence of infection; and (5) at least one previously successful pregnancy.

Where an appreciable number ofwomen had been observed without an infantile failure, the criteria were relaxed to include 61 women whose infections were of less than 2 years' duration and who showed no physical evidence of active infection even if they had positive serologic tests in low dilution. Each mother in the series had a quantitative serologic test for syphilis (STS) and a physical examination at monthly intervals throughout the pregnancy during which treatment was omitted. This was considered to be essential in order to detect at once any evidence of reactivation of the original maternal infection or any sign of reinfection. All infants were followed with serial serologic and physical examinations and, where possible, with serial roentgenograms, according to the usual procedure for the diagnosis of infantile congenital syphilis.

None of the infants of these patients treated with arsenic before the observed pregnancy showed evidence of syphilis. Although there were 48 abortions and stillbirths, these were attributable to obstetrical or medical cause other than syphilis. Similar results were reported by Barnett and Read (20) in their observations of 218 nonsyphilitic infants born of mothers treated with metal chemotherapy prior to the observed pregnancy and subsequently untreated.

Mothers Initially Treated With Penicillin

The results of withholding treatment from women originally treated with penicillin are equally good. As reported by Speiser and his associates (1), Ingraham (21), and Tucker (22), observations have now accumulated on 224 syphilitic women

initially treated for syphilis 3 with penicillin and allowed to go through subsequent pregnancies without further treatment (table 1).

Of their 249 observed pregnancies, 224 resulted in live, nonsyphilitic births, with 2 congenitally syphilitic children. Both of the failures were due to infectious relapses in the mothers, undetected until after delivery because the two women failed to return for the necessary monthly examinations in the last months of pregnancy. They represent failure of cooperation by the patients rather than of the plan of treatment: Twenty-three of the pregnancies (9 percent) terminated unsuccessfully in abortion, stillbirth, or neonatal death attributable to causes other than syphilis or previous therapy.

The 224 women were treated with varying amounts of penicillin. Nearly half were treated with 1.2 million units, a few with 600,000 units, and 40 odd with doses larger than 3 million units. Like the patients in the arsenic-treated group, they were carefully checked at monthly prenatal examinations for evidences of serorelapse, seroresistance in high titer, clinical relapse, or reinfection. Fifty-eight were seropositive during the untreated pregnancy in low and sustained titer, but delivered nonsyphilitic infants. The two infected infants described above were born to two of the seropositive women; both mothers lapsed from observation during pregnancy and so lost the opportunity for re-treatment.

It is felt that seropositivity in the mothers is not, per se, an indication for re-treatment.

Summary of Studies of Mothers Not Re-treated

Thus, observations are now available on 587 women previously treated for syphilis and followed in 819 pregnancies during which treatment was withheld (table 1). Two of the 749 living infants proved

³ In 87 percent of the group the original diagnosis was either primary or secondary syphilis; in the remainder, the original diagnosis was early latent, symptomatic late, or asymptomatic late syphilis.

to be syphilitic—a failure rate of 0.2 percent. Seventy-one of the pregnancies (8.7 percent) were unsuccessful due to abortion, stillbirth, or neonatal death not the result of infection with syphilis.

On the basis of these results, we can recommend without equivocation that it is not necessary to administer antisyphilitic treatment to a syphilitic woman during every pregnancy and that treatment may be withheld if: (1) the mother had previously received 4.0 gm. or more of arsphenamine or its equivalent, plus bismuth therapy; or at least 2.4 million units of aqueous penicillin or its equivalent; (2) the mother shows no clinical signs of active infection; and (3) the mother is seronegative or, if still seropositive, in a low titer only.

These recommendations are valid regardless of the stage and duration of infection in the mother at the time of her original diagnosis and treatment and regardless of the interval between the previous treatment and the pregnancy in which treatment is to be omitted. The time intervals between treatment and pregnancy in the arsenic group varied from less than 1 year to more than 20 years; in the penicillin group, the intervals were, for obvious reasons, less than 4 years.

Treatment of Congenital Syphilis

With penicillin so readily available, the incidence of congenital syphilis should rapidly approach the vanishing point. As has been repeatedly pointed out, the time to treat congenital syphilis is prenatally, when infection of the fetus may be entirely prevented or at least treated at the optimum time.

Diagnostic Follow-Up

In order to detect the cases of congenital syphilis that will, for a time at least, continue to be found (usually the result of delinquencies in prenatal observation of the mother), the offspring of syphilitic parents should be followed for a minimum of 4 months after birth. The follow-up should include a monthly quantitative blood serologic test, careful physi-

cal examination, and roentgenogram of the long bones between the fourth and the sixth weeks when possible.

Healthy infants born of mothers with positive blood serologic tests for syphilis may show transient positivity themselves, an indication of transmitted maternal reagin and not necessarily an indication of infantile infection. The passively transferred reagin will decline steadily and will disappear from the noninfected infant's blood within 4 months after birth (23). If the child is infected, positivity will be sustained or will increase and will be associated with confirmatory signs of congenital syphilis. In the presence of increasing or sustained positivity or when the course of maternal infection has been unfavorable, weekly examinations of the offspring are desirable so that treatment may be given to the infant at the optimum time.

A completely negative examination at the age of 4 months is a guarantee that the infant has escaped congenital infection.

Recommended Treatment for Infants

In the treatment of congenital syphilis, penicillin is the best single therapeutic agent so far employed, just as it is the most effective antisyphilitic drug for treatment of all forms of syphilis in adults. However, contrary to the situation in adult syphilis, the rules for the use of the drug in the infantile disease depend on data derived from clinical observations in relatively few cases. There are only 284 infants and children in Platou's (24) recent careful study. This is the largest single series reported to date, but the number is insignificant when compared with the thousands of observations of adults that have contributed to the evaluation of treatment schedules employed in adults.

It is clear that penicillin is responsible for dramatic effects in healing the florid lesions of congenital syphilis, but, particularly with young infants, it is important to remember that time and nonspecific pediatric therapeutic measures play a major role in therapy. It is still necessary to evaluate by more extensive studies a variety of schedules, vehicles, and routes of administration, as well as the possible combination of penicillin with other drugs, in order to discover the optimum method of therapy for children (24).

Aqueous penicillin.—The recommended schedule employing aqueous penicillin is a total dose of 100,000 units per kilogram of body weight, given in 120 injections at 3-hour intervals for 15 days. Vigorous supportive therapy is essential in infants because of the frequent association of severe intercurrent infections with syphilis, but there seems to be no justification for schedules of gradually increasing doses at the onset of the therapy. Furthermore, the reactions from the use of the drug have not seemed dangerous. Febrile reactions with elevations of temperature of from 1° to 3° during the first 36 hours after the onset of the treatment occur regularly in about half the infants Other reactions are insignifitreated. cant, despite the early fears on this subject.

careful analysis of the infants treated at the Johns Hopkins Hospital who might have been considered to have died as a result of penicillin therapy shows that there were always complicating and usually serious associated factors such as meningitis, unrecognized pneumonia, severe anemia, and fluid im-These deaths were not due to balance. the administration of penicillin and do not account for the mortality rates of between 5 and 10 percent for infants with congenital syphilis. Platou agrees with other observers that the "mortality rate is a reflection of the socioeconomic environment from which the patients are derived" rather than an indictment of penicillin (24).

Delayed-absorption preparations.—The recent literature on the use of delayed-absorption preparations of penicillin suggests the obvious desirability of using them for children because of the difficulty of giving multiple injections to marasmic or malnourished infants with au inadequate muscle mass. Clinical

trials on a small scale are now being made in several clinics, with procaine penicillin being administered in doses of 100,000 to 300,000 units daily in single injections for from 10 to 15 days. It would seem desirable to extend the series as rapidly as possible in order that the treatment schedules may be routinized.

The results of the use of penicillin in the infantile disease are considered satisfactory in nearly 90 percent of all the patients followed for more than 2 months and in nearly 100 percent of the infants treated before 3 months of age (25). Relapses have occurred in approximately 6 percent of the patients treated so far, and all of the relapses have responded satisfactorily to re-treatment with penicillin.

Treatment for Late Congenital Syphilis

In late congenital syphilis, the treatment schedules are approximately the same as those in adult patients. The results of treatment are more difficult to evaluate, because clinical signs of the disease are present in only one out of eight patients with late congenital syphilis; because of the inherent trend in these patients toward serologic negativity when no treatment is given; and because of the need for prolonged periods of posttreatment observation before the results of the therapy can be determined. The earlier treatment is given, the better the results, which is comparable to the situation in infantile and adult syphilis; results are probably better also if no previous treatment has been given of another sort. No deaths due to the use of penicillin have been reported in late congenital syphilis. Febrile reactions occur in about 40 percent of the older children during the first 48 hours after the drug is started (24).

In congenital neurosyphilis, the results of the use of penicillin are probably as good as any previously described, and

⁴ The term "satisfactory" means a continued state of well-being, the disappearance of reversible lesions, and a progressively declining titer.

perhaps better, although there are no extensive comparative studies available. In interstitial keratitis, the small number of patients treated makes it impossible to draw any valid conclusions regarding treatment results, and they probably are not very encouraging (26). It is important in this connection to remember that therapy should be begun as early as possible after the onset of the eye involvement. Various other lesions of the late disease have been reported as responding relatively well to treatment with penicillin.

Summary

In summary, the following rules are outlined to provide for the care of syphilitic pregnant women and children who have congenital syphilis:

1. Penicillin is the drug of choice for treatment.—

In treating the syphilitic pregnant woman—

- 2. When aqueous penicillin is used, a total dose of at least 2.4 million units should be employed, given in doses of 40,000 units every 3 hours for a total of 60 intramuscular injections.
- 3. When completely ambulatory treatment is essential, POB may be given in total dosage of at least 4.8 million units, either with daily injections of 600,000 units each for at least 8 days or with 300,000 units daily for 15 days.⁵
- 4. With the use of procaine penicillin G in oil containing 2 percent of aluminum monostearate, it is likely that an adequate schedule is one of 1.2 million units once a week for from 2 to 4 weeks (a total of from 2.4 to 4.8 million units). Another possible schedule is 1.2 million units in a single injection.
- 5. It is not necessary to administer antisyphilitic treatment to a syphilitic woman during every pregnancy. Treatment may be withheld if the mother has previously completed "adequate" therapy with arsenic and bismuth or with peni-

cillin, if she shows no clinical signs of active infection and if she is seronegative, or, if still seropositive, in a low titer only.

In treating infants and children who have congenital syphilis—

- 6. When aqueous penicillin is used, a total dose of 100,000 units per kilogram of body weight should be employed, administered in 120 injections at 3-hour intervals. A tentative schedule using procaine penicillin is one of from 100,000 to 300,000 units daily for from 10 to 15 days.
- 7. Careful prenatal and postnatal observations are still essential. When this is impossible, more conservative methods of treatment are necessary. Since penicillin offers great hope for the infant with little or no risk to the mother, when in doubt, treat.

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How To Evaluate Positive Kahn Tests in Infants¹

Herman N. Bundesen, M. D.,² and Hans C. S. Aron, M. D.³

The incidence of positive serologic tests not indicative of syphilis is higher in infancy than at any other age. In infants born of penicillin-treated syphilitic women, the positive serologic tests not indicative of congenital syphilis outnumber many times the positive tests indicating congenital syphilis (1, 2). Even several positive serologic tests in infants do not permit the diagnosis "syphilis" or the initiation of antisyphilitic therapy. In every case where a serologic test for syphilis is found to be positive in an infant, careful investigation should be made to find the cause.

During follow-up studies of infants born of syphilitic mothers treated at the Chicago Intensive Treatment Center, some interesting observations were made. This experience constitutes the basis of approach to the intricate problem of evaluating positive serologic tests for syphilis in infants.

The great majority of these positive tests are due to the presence of true syphilitic reagin in the infant's blood, but this syphilitic reagin is of maternal origin. The maternal reagin, transmitted from the mother's blood through the placenta to the fetus, remains in the blood of the newborn infant for some time after birth. This phenomenon of passive transfer or transmission of reagin was reported 35 years ago (3), has been discussed in the literature (4-10), and is described in pediatric textbooks (11-12), but it is still

not sufficiently familiar to many physicians. Not infrequently, healthy non-syphilitic infants have been misdiagnosed as syphilitic in the past (13–15) and, from our experience, the same misdiagnosis is still made occasionally.

Positive serologic tests for syphilis in the blood of healthy infants due to the passive transfer of reagin from the mother can be recognized readily by the following characteristics:

- 1. Repeated clinical examinations of the infant and X-ray films of the long bones reveal no signs of congenital syphilis.
- 2. The quantitative titer of the infant's blood is low, usually lower than the titer of the mother's blood. The titer in the infant's blood never rises. On the contrary, it declines spontaneously until negative, usually within 90 days, and remains negative permanently.

An identical pattern of serologic tests may be found in infants who were infected and successfully treated in utero by penicillin given to the mother during the last months of pregnancy. In most instances it is difficult to make the diagnosis of intra-uterinely cured syphilis with any degree of certainty. (The diagnosis of intra-uterinely cured congenital syphilis can be substantiated when it is possible to show: (1) that the titer in the infant's blood at birth or shortly thereafter is considerably higher than the titer of the mother's blood obtained simultaneously, and (2) that X-ray films of the long bones reveal definite evidence of healing osteochondritis and/or perios-As long as the serologic tests of these infants become spontaneously negative and remain negative, the infants require no antisyphilitic therapy and may be classified temporarily with the group of infants with positive tests due to passive transfer of reagin.

¹From the Chicago Intensive Treatment Center, Venereal Disease Control Program, Chicago Board of Health, in cooperation with the U. S. Public Health Service. Read at the Chicago Venereal Disease Control Seminar, February 16, 1950.

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Figures 1 and 2 demonstrate how the passive-transfer pattern of a series of quantitative serologic tests differs from the pattern of tests observed in infants developing congenital syphilis. Figure 1

shows three typical cases of infants with positive tests due to passive transfer, and figure 2 shows three typical cases of infants who developed unquestionable congenital syphilis.

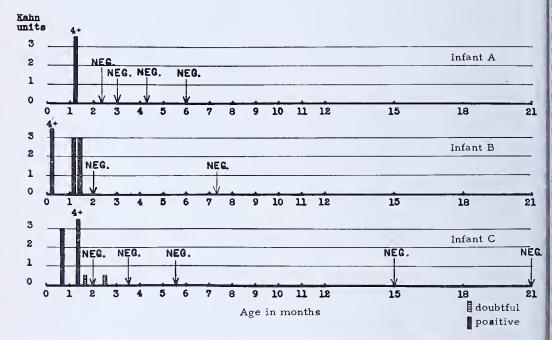


FIGURE 1.—Serologic test patterns of three infants having positivity due to passive transfer of mother's reagin.

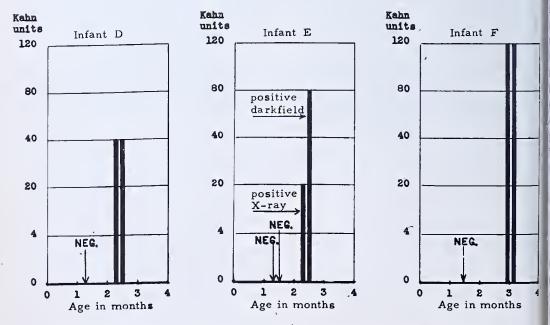


FIGURE 2.—Serologic test patterns of three infants who have congenital syphilis.

The passive-transfer pattern is characterized by a moderately low quantitative titer that does not rise but declines spontaneously to negativity and remains negative. In the syphilitic pattern, tests are frequently negative at birth. may remain negative for from 4 to 12 weeks, then suddenly become positive, and almost invariably show a steep rise to high titers. X-ray films may reveal definite evidence of congenital syphilis while the Kahn test is still negative (16). Usually, but not in all instances, clinical signs of congenital syphilis develop after the Kahn tests become positive with a rising titer.

Paradoxical as it may appear, an infant with negative serologic tests who thereafter develops positive tests is much more a suspect of congenital syphilis than is an infant with positive serologic tests at birth or during the first weeks of life.

However, the fact that an infant of a syphilitic mother, after several negative serologic tests, suddenly develops positive tests is not sufficient to establish the diagnosis of syphilis. There may be other causes than syphilis for these positive tests. During our follow-up studies, unexpected positive Kahn tests were reported several times for apparently healthy infants who previously had had one or more negative Kahn tests. While this event at first appeared highly suspicious of syphilis, it was perplexing that neither physical examination of the infants nor X-ray films of the long bones showed signs indicative of congenital syphilis. When closely scrutinized, the pattern of these positive Kahn tests was found to deviate from the typical syphilitic pattern in two essential points:

- 1. The quantitative Kahn titer was comparatively low (2 to 4 units) and the titer did not rise when the test was repeated.
- 2. The first positive Kahn test did not appear until the infants were 5 months of age or older. Negative tests had been recorded when the infants were 3 months of age.

Evaluating these factors made it highly

probable that the positive serologic tests had to be regarded as biologic false-positive tests. This opinion was confirmed by the fact that after several weeks the positive tests spontaneously reversed to negative and remained negative.

In the cases of infants G and H, the positive tests could be traced to smallpox vaccinations performed 3 and 6 weeks previously. Infant I was a 91/2-month-old infant with numerous scars typical of chickenpox. Three consecutive positive Kahn tests were found 3 to 6 weeks after the outbreak of chickenpox. The Kalın tests repeated 2 and 5 months later were negative. These three examples are demonstrated in figure 3. Biologic falsepositive Kahn tests in adults after vaccination and after chickenpox have been reported in the literature (17, 18).

Other remarkable causes for biologic false-positive Kahn tests are shown in figure 4. Infants J and K revealed no clinical or X-ray findings of congenital syphilis and had several negative Kahn tests. They developed positive Kahn tests of 3 and of 2 units, respectively, at the age of about 5½ months. Both of these infants had been given pertussis immunization 3 and 5 weeks previous to the positive Kahn Since in both instances the serologic tests spontaneously reversed to negative and remained repeatedly negative for 18 months, we have here biologic false-positive serologic tests following pertussis immunization.

The third infant shown in figure 4 had had negative tests following the three pertussis immunization procedures. Four weeks after completion of a course of diphtheria immunizations, this infant showed a positive Kahn test of 3 units. When repeated 3 weeks later, the Kahn test was still 3 units positive. But without any therapy, the Kahn tests reversed to negative and remained negative. The absence of any clinical symptoms suspicious of syphilis, together with the course of the series of Kahn tests, definitely warrants the diagnosis of biologic falsepositive tests following diphtheria immunization.

These observations are additions to

the long list of causes for biologic falsepositive serologic tests for syphilis (19– 25). Since all infants should be subjected to smallpox vaccination and to immunization against pertussis and diphtheria, the possibility that these procedures may occasionally cause biologic false-positive serologic tests should be

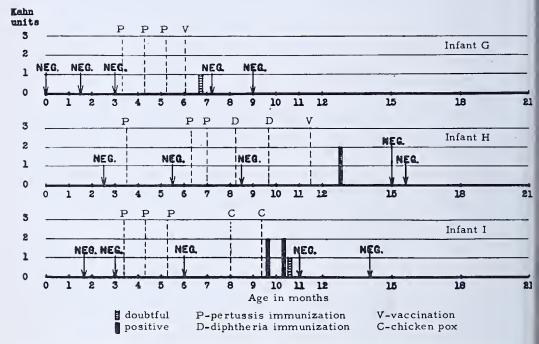


Figure 3.—False-positive serologic test patterns of three infants after vaccination and after chickenpox.

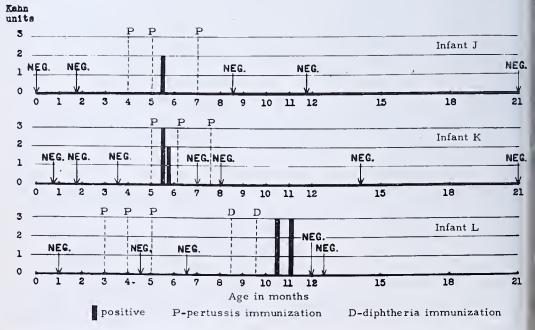


Figure 4.—False-positive serologic test patterns of three infants after immunization for pertussis and diphtheria.

kept in mind. It is especially important to remember this possibility when serologic tests are made of infants born of known syphilitic mothers.⁴

In discussing biologic false-positive serologic tests for syphilis, Moore (13) makes the following statement:

"A few cases adequately controlled, with negative tests before the onset of an acute infection, positive tests for a variable period of time, followed by permanent seronegativity following the subsidence of the infectious process, would be of more value than several hundred cases tested at random."

The observations presented here fulfill those postulates of adequate control. For this reason, it was thought worth while to report them in detail.

Summary and Conclusions

In infants, even repeatedly positive serologic tests are not sufficient to establish the diagnosis of syphilis or to initiate antisyphilitic therapy. Several causes besides congenital syphilis may be responsible for the appearance of positive serologic tests for syphilis in infants. In every case where a positive serologic test is found in an infant, a careful attempt should be made to evaluate its meaning.

The majority of positive tests found during the first months of life are due to a passive transfer of maternal reagin during pregnancy from the mother to the fetus. This reagin remains in the in-

fant's blood for some time after birth and repeated serologic tests reveal a typical transfer pattern in which the quantitative titer is comparatively low, does not rise when the test is repeated, declines spontaneously, and remains negative permanently.

The syphilitic pattern, as observed in infants who develop unquestionable congenital syphilis, is distinctly different. In many of these syphilitic infants, the serologic tests are negative up to from 4 to 12 weeks of age, suddenly become positive, and almost invariably rise rapidly to high titers.

Biologic false-positive Kahn tests in infants born of known syphilitic mothers were observed in two infants after vaccination, in one infant after chickenpox, in two infants after pertussis immunization, and in one infant after diphtheria immunization.

These biologic false-positive tests, appearing after previous negative tests, could be differentiated from true syphilitic tests in that the infants did not reveal any evidence of congenital syphilis and in that the titer was comparatively low (4 units or less) and did not rise when repeated. The first positive Kahn test did not appear until the infants were 5 months of age or older. The positive tests reversed to negative spontaneously and remained negative, thus confirming the diagnosis of biologic false-positive tests.

The evaluation of positive serologic tests for syphilis in infants requires repeated quantitative tests. The criteria developed in this article permit the recognition of:

A. Positive tests *not* indicative of syphilis:

- 1. Caused by passive transfer of reagin from mother to child, encountered from birth to the third month of life.
- Biologic false-positive tests after infectious disease, vaccination, or immunization, mostly observed after the third month of life.

B. Positive tests typical of congenital syphilis.

⁴ In two instances, biologic false-positive Kahn tests were observed in children during their second year of life. Both were children of known syphilitic mothers. While presentng an extended impetigo, a 221/2-month-old girl had a positive Kahn test of 1 unit. Four Kahn tests taken previously had been nega-When the impetigo had practically lealed, the Kahn test was negative. Another girl had negative Kahn tests at the ages of 3 and 7 weeks and at 7, 91/2, and 16 months; she had measles when she was 17 months old, followed by an upper respiratory infection; it the age of 22 months, her Kahn test was positive (2 units); Kahn tests taken at the iges of 24 and 28½ months again were negative.

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The Dentist's Role in Finding Congenital Syphilis

Frank P. Bertram, D. D. S., M. P. H.1

It is increasingly apparent that the lental profession is a link in the control hain of congenital syphilis. According o Jeans (1), the dental deformities contitute the most important of the stignata of congenital syphilis due to their elative frequency. Of 463 syphilitic chillren over 6 years of age, he noted dental ypoplasias in 185 (40 percent). From our experience, a diagnosis based on "typcal" Hutchinson's teeth is too restrictive. The gross abnormalities are readily aparent, but dentists, because of their raining and clinical experience, are lighly conscious of slight dental variaions. This is important in the detection f atypical manifestations and in the diferentiation of Hutchinson's teeth from ther dental hypoplasias. Brauer and Blackstone (2), two dentists, reported a igher percentage of dental dystrophies ssociated with congenital syphilis than ther observers have reported. It seems articularly important for public health entists to be alert to the contribution hey can make in the field of venereal disase control.

Rapid dental surveys, although a reent development, are gaining recognition s a useful case-finding technic among a groups in which syphilis is most comion. Dental inspections at the rate of 00 an hour, however, are nothing more an a screening process. Attention is oncentrated on the permanent incisor and first molar teeth, since anomalies of the type for which we are looking may be lost easily detected in these teeth.

Oklahoma Study

In the dental study made in Oklahoma 3) in 1948, the majority of the Negro ildren examined were of elementary thool age, since it was felt that the probbility of finding primary infection in

children so young would be sufficiently remote as to have no material effect on the data.

Oklahoma City Series

In the first phase of the study, a group of Oklahoma City elementary school children were screened and given blood tests. Dental inspections were made of 1,045 children in the first through the sixth grades, the average age being 9.25 years. The blood testing was on a voluntary basis, and 628 (60 percent) of the children had blood tests. Eight of the 628 children had a positive serologic test for syphilis (STS), giving a prevalence of 1.3 percent for the group. Of the 1,045 children inspected, 26 were diagnosed as having Hutchinson's teeth, a rate of 2.5 Sixteen of these 26 children were among the 628 children who were given a blood test. Of these 16 children, 4-one-fourth of the group-had a positive STS. Granting the fallacy of drawing conclusions from 16 cases, there is still a significant difference between the rate of 25 percent for the selected group and 1.3 percent for the group as a whole. Stated differently, of the 8 children whose blood tests were positive, one-half could have been found by testing 16 dentally screened children.

Oklahoma State Series

In the second phase of the study, serologic tests for syphilis were performed only on the children who were diagnosed as having Hutchinson's teeth. The work was done in seven schools scattered throughout Oklahoma. In three of the seven schools, high school students were included in order to obtain enough children. The average age of the entire group was 10.2 years, nearly a year more than the average age of the children in the Oklahoma City series. From the dental screening of 1,111 students, a diagnosis of Hutchinson's teeth was made in 43 in-

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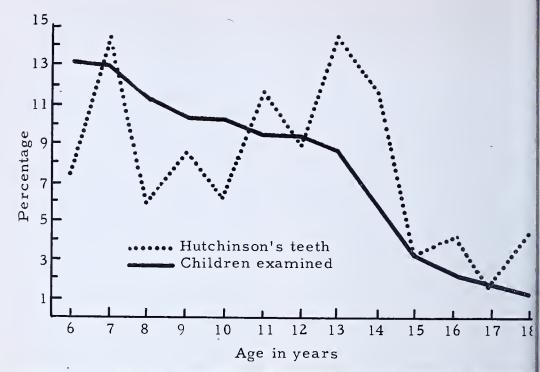


Figure 1.—Percentage age distribution of 2,156 children dentally screened for congenital syphilis and of 69 who were diagnosed as having Hutchinson's teeth.

stances, a rate of 3.9 percent. Of these 43 children, 37 were given a blood test, and 9—almost one-fourth of the group—were found to have a positive STS.

Combined Series

Combining the data from the two series, of 2,156 dental inspections, 69 children (3.2 percent) were diagnosed as having Hutchinson's teeth; 53 of the 69 children were given a blood test, and 13 (24.5 percent)² were found to be positive. The percentages of positive blood tests in the two groups are strikingly similar—25.0 percent in the Oklahoma City group and 24.3 percent in the Oklahoma State group.

The percentage age distributions of the 69 children with Hutchinson's teeth and of the 2,156 children who were given a dental inspection are shown in figure 1. The age range of the children was from 6 to 18 years, and 12 years was taken as the mid-point. The occurrence of Hutchinson's teeth was proportionately higher

in the older children (13 to 18) than i the younger children (6 to 12). Assun ing that the 12-year-old children were bor during 1936—the year in which the intersive venereal disease control program started—the smaller proportion of Hu chinson's teeth found in the younge group presumably reflects the effectiveness of the control program.

Education and legislation on prenata blood testing are powerful control factors The sustained campaign waged agains venereal disease during the past decad or more is, as we have seen, being fe now in a reduction of congenital syphili The fact remains, however, that amon the colored population, where the rate (syphilis is high, our prenatal control i poor. Many colored women are not see by midwife or physician until the time of delivery, rendering prenatal blood testin an impossibility. It is probable, there fore, that congenital syphilis as a problem of considerable proportions will remai with us for some time, with the dents profession making its contribution to the eventual solution.

² This percentage has a standard error of slightly less than 6 percent.

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CURRENT NOTES AND REPORTS

International Serodiagnostic Conference To Be Organized by WHO

The World Health Organization is accepting applications from author-serologists who wish to participate in an international serodiagnostic conference to be held sometime after October 1951. Dr. Peter Krag, previously Director of the Serological Department of the State Serum Institute in Copenhagen, has accepted assignment with the WHO to direct the conference, the site of which will be announced later.

International serodiagnostic conferences have been held by the League of Nations, 1923 and 1928 in Copenhagen, 1930 in Montevideo, and by the United States Public Health Service, 1941 in Washington, D. C. In 1939, a similar conference planned in Copenhagen was cancelled at the outbreak of the war.

These conferences contributed significantly to the technical development and standardization of serologic methods and intigens in the diagnosis of syphilis. It has been recognized that conferences of his kind are the only means of comparing efficiency in test methods, of which is many as twenty different ones were compared at international serodiagnostic conferences in the past, at the same time offering a rare opportunity for exchange of scientific technical information between test-authors.

The Interim Commission of the WHO (1947) and its Advisory Committee on Venereal Diseases pointed out the necessity of holding further serodiagnostic standardization conferences. The First

(1948) and Second World Health Assemblies (1949) emphasized the need for further standardization of serodiagnostic laboratory procedures inan towards greater uniformity in serologic The Sub-Committee test performance. on Serology and Laboratory Aspects of WHO 1949, considered in its report an outline for the conference to be held in 1951 or 1952. This outline was approved by the fifth session of the WHO Executive Board along with the other activities of WHO under the laboratory program of the organization. The planning of the laboratory conference has since gone forward actively.

Taking into account the continued use in all parts of the world of a great variety of seroreactions, with often divergent results; the appearance several new serodiagnostic tests which were not evaluated at previous international laboratory conferences; the development of purified cardiolipin-lecithin antigens (Pangborn); the Treponema immobilization reaction (Nelson); and the general need for determining the most useful and practical serodiagnostic methods for mass serologic examination, the Director-General of the World Health Organization has invited authors of methods for the serodiagnosis of syphilis to register preliminary applications for admittance to the WHO Serodiagnostic Laboratory Conference. Applications are to be received by WHO before July

CURRENT LITERATURE

AM. J. M. Sc., PHILADELPHIA

The etiology of pulmonary arteriosclerosis (Ayerza's syndrome). With report of an illustrative case. Simon S. Leopold. Am. J. M. Sc., 219: 152-160, Feb. 1950.

In this review of the literature, with the presentation of a case report which fulfilled the essential diagnostic data and which at necropsy showed changes in the aorta compatible with syphilis, the author thinks that the condition occurs most frequently in an individual with syphilitic infection who has, in addition, a chronic infection of the lower respiratory tract.

AM. J. OBST. & GYNEC., ST. LOUIS

An improved treatment for *Trichomonas* vaginalis vaginitis. John F. Fiorino, Louis Arrigoni, and G. A. Tozer. Am. J. Obst. & Gynec., 59: 452–454, Feb. 1950.

Three hundred patients were treated with a buffer acid douche to lower the pH to the normal range, followed by an insert composed of acid buffer salt and a wetting agent which maintains the normal vaginal acidity. Of 279 who returned for reexamination, 268 were cured without recurrence and the other 11 were cured after additional treatment.

Brit. J. Radiol., London

Gummatous stenosis of the bronchus. Frank L. Ingram. Brit. J. Radiol., 23: 116-118, Feb. 1950.

A brief description is given of the X-ray appearances of pulmonary syphilis with a case of gummatous stenosis of the right upper lobe bronchus with collapse of the lobe.

Bull. Georgetown Univ. M. Center Washington

Some practical considerations in the diagnosis and treatment of syphilis. Pasquale J. Pesare and Mario Mollari. Bull. Georgetown Univ. M. Center, 3: 194–202, Feb.–Mar. 1950.

Discussion is given on diagnosis and

treatment of syphilis in pregnancy, congenital, early infectious, latent, central nervous system, and cardiovascular syphilis. Notes are presented on infectiousness as well as recent advances in syphilology. Statistics are given which show gains made in control.

Bull. School Med. Univ. Maryland, Baltimore

Present status of aureomycin and chloramphenicol therapy. Theodore E. Woodward, Robert E. Bauer, Robert T. Parker, and Howard E. Hall. Bull. School Med. Univ. Maryland, 35: 8-12, Jan. 1950.

A review is presented of information thus far attained concerning use of these drugs in various infections, including gonococcic urethritis and lymphogranuloma venereum. Dosage and toxicity are considered.

CHRON. WORLD HEALTH ORGAN., GENEVA

New developments in venereal disease control. Third session of the Expert Committee on Venereal Infections. Chron. World Health Organ., 4: 35-40, Feb. 1950.

Committee discussed control technics, antibiotic therapy in syphilis and other treponematoses, serologic and laboratory aspects of venereal disease infections, and the report of the WHO Syphilis Study Commission to the United States.

Serology of syphilis. Chron, World Health Organ., 4: 41-45, Feb. 1950.

Subcommittee on Serology and Laboratory Aspects of the Expert Committee on Venereal Infections devoted major part of discussion of its first session to question of the International Serological Laboratory Conference which WHO proposes to convene in 1951 or 1952. General plans for the conference are discussed.

Venereal disease control in the USA. Report of the WHO Syphilis Study Commission. Chron. World Health Organ., 4: 67-76, Mar. 1950.

CHRON. WORLD HEALTH ORGAN. GENEVA—CONTINUED

A report of the Commission as discussed by the Expert Committee on Venereal Infections during its third session, October 1949, in Washington, D. C., describes the history and present organization of control in the United States, research, education, epidemiologic factors in control, treatment, measures against introduction of syphilis into the States, trend of syphilis, and comments by the executive board.

GLASGOW M. J., GLASGOW

The importance of the tongue as an index of disease. Alastair McCrone. Glasgow M. J., 31: 45-69, Feb. 1950.

The pathology of the tongue in syphilis is included in this general discussion.

INDIAN J. VEN. DIS., BOMBAY

Gonococcal infection of the median raphe. R. V. Rajam and H. Vasudeva Rao. Indian J. Ven. Dis., 15: 123-124, Oct.-Dec. 1949.

Case history is given of a Hindu who had discharge of pus containing gonococci on ventral aspect of skin of penis.

Modern concepts of syphilis control. John C. Cutler, Johs Kvittingen, R. Balachandran Tampi, Evelyn Rose, and George M. Leiby. Indian J. Ven. Dis., 15: 128-139, Oct.-Dec. 1949.

Outline of history, diagnosis, serology, medical management, public health aspects, and prophylaxis of syphilis is presented, as published by the Health Department, Government of West Bengal.

Incidence of syphilis in the remotest hills of Himachal Pradesh. Bishamber Das Chowhan. Indian J. Ven. Dis., 15: 139–141, Oct.—Dec. 1949.

Incidence is high among povertystricken people of the hills of India. Absence of pain is blamed for incidence where illiteracy and blind faith are firmly cotted.

INDIAN M. GAZ., CALCUTTA

V. D. control in S. E. Asia. Indian M. Gaz., 84: 561–562, Dec. 1949.

A plan is described for establishing a renereal disease control program for In-

dia and a training center to train doctors, laboratory technicians, nurses, and public health workers. These plans were set forth by WHO.

INTERNAT. HEALTH BULL, LEAGUE RED CROSS SOCIETIES, GENEVA

The medical service as part of the relief work of the League of Red Cross Societies for Palestinian refugees. Haldord Larsen and Z. S. Hantchef. Internat. Health Bull. League Red Cross Societies, 1: 8–20, Oct.—Dec. 1949.

In discussing general medical service, it is said that little is known relative to incidence of syphilis, since there is little opportunity to make blood tests. At one seminomadic refugee camp where blood tests were made on 352 women, 16 were positive.

J. INDIAN M. A., CALCUTTA

Venereal disease in industry. Sunil Kumar Das. J. Indian M. A., 19: 131-134, Jan. 1950.

Steps which could be taken by the government, the labor unions, industrial management, and the health department to lower the high venereal disease rate among laborers are discussed. Attendance records from the clinics of West Bengal during 1947 indicated that 40.5 percent of those receiving treatment for venereal disease were laborers.

J. Invest. Dermat., Baltimore

Neurosyphilis: comparative treatment with penicillin alone and penicillin plus malaria. William F. Spiller and John Stewart. J. Invest. Dermat., 14: 121– 131, Feb. 1950.

This study, performed at the Cleveland City and University Hospitals, included 170 patients with neurosyphilis who were treated with penicillin and penicillin plus malaria and observed for from 6 months to 4 years. In various types of neurosyphilis the spinal fluid findings responded equally well on both schedules of treatment and the clinical response of symptomatic neurosyphilis was broadly the same with penicillin as with penicillin and malaria.

J. NERV. & MENT. DIS., NEW YORK

An evaluation of vitamin E therapy in diseases of the nervous system. Simon Stone. J. Nerv. & Ment. Dis., 111: 139-146, Feb. 1950.

Vitamin E therapy is of limited value when used alone in treating tabes dorsalis. In combination with vitamin B complex, orally and intraspinally, it is of definite value in bringing about improvement of gait and arresting the progress of cord degeneration.

LANCET, LONDON

Comparative serum testing with cardiolipin and standard Wassermann antigens. Review of 5,124 tests. I. N. Orpwood Price and A. E. Wilkinson. Lancet, 1: 14–16, Jan. 7, 1950.

A comparison of cardiolipin antigen with standard Wassermann antigen by the parallel testing of 5,124 serums, using a modified Harrison-Wyler technic, showed cardiolipin antigen to be more sensitive than the standard. The cardiolipin test showed a higher proportion of cases of early primary syphilis and remained positive in treated patients after other tests had been reversed to negativity.

Penicillin in tissue exudates after injection. J. Ungar. Lancet, 1: 56-59, Jan. 14, 1950.

The author demonstrated with intramuscular injection of penicillins G, F, and K in rabbits, that detectable amounts of the drug remain in the fluid of damaged tissue about twice as long as in the blood stream. This selective accumulation of penicillin in the inflamed area is one of the most important factors in the therapeutic effect of single massive doses of penicillin.

NAT. NEGRO HEALTH NEWS, WASHINGTON

A cooperative plan for health education and venereal disease control. Edward A. Benjamin. Nat. Negro Health News, 18: 9– 10, Jan.-Mar. 1950.

Article tells of newer philosophy of venereal disease control and how it is applied. It also describes a health education demonstration for a teacher education institution.

OREGON HEALTH BULL., PORTLAND

Downward trend indicated in State venereal incidence. Samuel B. Osgood. Oregon Health Bull., 28: 3, Feb. 1, 1950.

A 5-year average syphilis morbidity rate of 129.2 per 100,000 population was reached in Oregon in the period 1942–48. The present level of incidence is similar to that obtained in 1934–35.

OVERSEAS POST-GRAD. M. J., LONDON

Advances in the treatment of heart disease. Graham W. Hayward. Overseas Post-Grad. M. J., 4: 199-204, Jan. 1950.

A review is presented of some of the more important advances among which is the treatment of syphilitic aortitis with penicillin.

Angiocardiography. Frances Gardner. Overseas Post-Grad. M. J., 4: 215-226, Jan. 1950.

The author discusses an established diagnostic procedure of use in suspected cases of syphilitic aortitis, the picture showing a local bulging and loss of parallelism of the aortic walls,

PROC. Soc. EXPER. BIOL. & MED., UTICA

Phytotoxic properties of spinal fluids from paresis, tabes and neurosyphilis. David I. Macht. Proc. Soc. Exper. Biol. & Med., 73: 186-187, Feb. 1950.

Phytopharmacologic, examination of spinal fluids from paresis patients yielded phytotoxic results; from tabes dorsalis patients, the same as from normal spinal fluid; and other neurosyphilis patients yielded almost normal indices of growth.

PUB. HEALTH NEWS, TRENTON

Let's give babies a break. Theodore J. Bauer. Pub. Health News, 31: 54, Feb. 1950.

In presenting a picture of the status of congenital syphilis, the author stresses that it is preventable, and any age is too late to find it. Even with decline of syphilis cases, reported cases of congenital syphilis have remained constant for over 5 years.

SOUTH AFRICAN M. J., CAPE TOWN

Recent advances in venereology. James Marshall. South African M. J., 24:97-101, Feb. 11, 1950.

Recent advances in the last 50 years inlude improvement in type of therapy and reatment of heavy metal poisoning; emloyment of pyretotherapy as an adjuant to other treatment; and discovery of an infective agent as the cause of postresphenamine jaundice.

Penicillin in early syphilis. Results obtained in 365 cases. C. K. O'Malley.

South African M. J., 24: 127-132, Feb. 25, 1950.

Results of treatment using penicillin, arsenic, and bismuth on a 7½- or 8-day schedule at Cape Town City Hospital showed good results for primary syphilis but poor results for secondary syphilis. Of 86 patients followed for 12 months, 12 were treatment failures. Of 76 who had spinal fluid examinations 6 months following treatment, one showed doubtful reaction to Wassermann test, while all others were normal.

STATISTICS

Reported Cases of Congenital Syphilis, Fiscal Years 1941-50, by Quarters

[Civilian]

Period	Continental United States	United States, including Territories	Period	Continental United States	United States, including Territories
941: First quarter Second quarter Third quarter Fourth quarter	3, 936 4, 410 4, 866	4, 396 3, 949 4, 423 5, 184	1946: First quarterSecond quarter Third quarter Fourth quarter	2, 684	3, 453 3, 187 3, 683 3, 858
Total	17, 592	17, 952	Total	12, 106	14, 181
H2: First quarterSecond quarterThird quarterFourth quarterFourth quarter	4, 220 4, 180 4, 110	4, 763 4, 708 4, 513 4, 937	1947: First quarterSecond quarterThird quarterFourth quarter	3, 049	3, 473 3, 453 3, 589 3, 612
Total	16, 924	18,921	Total	12, 284	14, 127
H3: First quarter Second quarter Third quarter Fourth quarter Total	3, 861 3, 829 4, 078	4,824 4,349 4,229 4,540 17,942	1948: First quarterSecond quarterThird quarterFourth quarter	3, 140 2, 871 3, 398 3, 900	3, 480 3, 111 3, 668 4, 251
144: First quarter Second quarter Third quarter Fourth quarter	3, 630 3, 102 3, 442	4, 368 3, 450 3, 875 4, 014	1949: First quarter Second quarter Third quarter Fourth quarter	3, 536 3, 097 3, 702	3, 891 3, 500 4, 023 4, 253
Total	13, 576	15, 707	Total	14, 295	15, 667
45: First quarter Second quarter Third quarter Fourth quarter	2,853 3,006	3, 795 3, 361 3, 543 4, 031	1950: First quarter Second quarter Third quarter	3, 225	3, 546 3, 440 1 3, 776
Total	12, 339	14,730			

¹ Estimate.

Source: Form 8958-B FSA-PHS Division of Venereal Disease, Office of Statistics. 2/6/50 (ML-MC-EJD).



DOCUMENTS SECTION

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FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE

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Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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PUBLIC HEALTH SERVICE

LEONARD A. SCHEELE, Surgeon General

Editor: THEODORE J. BAUER, Medical Director Chief, Division of Venereal Disease

The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - - Price 15 cents. Subscription price: Domestic \$1.25 a year; foreign \$1.50

Eight Point Agreement of 1948

In November 1948, the Interdepartmental Committee on Venereal Disease submitted to the Treasury Department, the Department of Defense, the Federal Security Agency, and the Association of State and Territorial Health Officers the following agreement for continued cooperation in venereal disease control.

This agreement, which has been approved and signed by the official agencies, is a revision of a similar agreement of 1946, in which the same agencies participated.

An Agreement on Measures for the Control of Venereal Diseases, November 1948

It is recognized that the following services should be developed by State and local health and law enforcement agencies in cooperation with the Public Health Service of the Federal Security Agency, the Coast Guard of the Treasury Department, the Departments of the Army, Navy, and the Air Force of the National Defense Establishment, and interested voluntary organizations:

- 1. The Armed Services and the Coast Guard will provide early diagnosis and adequate treatment for military personnel infected with venereal disease.
- 2. Health departments will provide adequate case-finding, diagnostic, treatment, and case-holding procedures for the venereal diseases in the civilian population.
- 3. The civilian contacts of military personnel infected with venereal disease will be determined, and reported by officers of the Armed Services ¹ and the Coast Guard through medical channels to State and/or local health authorities only.
- 4. The military contacts of infected civilians should be reported to appropriate officers of the Armed Services and the Coast Guard by local or State health authorities.
- 5. Recalcitrant infected persons should be isolated during the period of communicability. In civilian populations it is a duty of local health authorities to obtain any needed assistance of the law enforcement authorities in enforcing such isolation.
- 6. The law enforcement authorities are responsible for the repression of commercialized and clandestine prostitution. In order to limit the spread of venereal infections from these sources, the local health departments and State health departments, the United States Public Health Service, the Armed Services, and the Coast Guard will cooperate directly or through Armed Forces Disciplinary Control Boards with law enforcement authorities in repressing prostitution and allied vice conditions, by providing them with the necessary available information relative to places and means of procurement and/or exposure, as may assist them in carrying out their responsibilities.
- 7. An aggressive continuous program of education should be carried on among military personnel and the civilian population regarding the dangers of promiscuous sexual conduct and venereal diseases, methods of preventing venereal infections, and the action which should be taken by a person who suspects that he is infected.

¹ Familial contacts of military personnel will be reported in accordance with existing Armed Forces directives.

8. State and Territorial health officers, the Public Health Service of the Federal Security Agency, the Coast Guard of the Treasury Department, the Departments of the Army, the Navy, and the Air Force of the National Defense Establishment, all invite the assistance of representatives of the American Social Hygiene Association, affiliated social hygiene societies, and of other official and voluntary welfare organizations or groups, in developing and stimulating public support for the above measures.

ulating public support for the above measures.

E. W. Foley, Jr.,

Secretary of the Treasury.

Louis Johnson,

Secretary of Defense.

J. Donald Kingsley,

Acting Federal Security Administrator.

R. H. Hutcheson,

President, Association of State and Territorial Health Officers.

Effectiveness of Penicillin in Preventing Congenital Syphilis When Administered Prior to Pregnancy

H. N. Cole, M. D., Frederick Plotke, M. D., M. P. H., Evan W. Thomas, M. D.;3 Kenneth H. Jenkins 4

An earlier report ⁵ discussed the efficacy of penicillin therapy in preventing congenital syphilis when administered first during pregnancy of the syphilitic mother. This study undertakes to provide information on whether supplemental penicillin therapy is necessary to prevent transmission of infection in the pregnant woman who has been "successfully" treated for syphilis prior to conception. Pooled records from three intensive treatment centers provided the data for both studies.

The earlier study was based on 414 outcomes of pregnancy from patients treated during pregnancy for primary, secondary, or early latent syphilis with amounts of aqueous penicillin varying from 200,000 to 9,600,000 units. A status based on clinical and serologic evidence was established at 90 days or later in 311 of the outcomes of pregnancy, and it was found that 11 of these (3.5 percent) were diagnosed as The summary showed that (a) best results were obtained from schedules using at least 2,400,000 units of penicillin; and (b) no syphilitic outcomes of pregnancy were noted in those mothers who had attained and maintained seronegativity prior to delivery.

The present study is based on 341 outfrompregnancy treated *prior* to conception with amounts of aqueous penicillin varying from 600,000 to 9,600,000 units (320 to 360 mg. of arsenoxide were administered in combination with penicillin to 58 of the patients). The group included 321 patients originally treated for primary or secondary syphilis and 20 originally treated for early latent syphilis. None had been re-treated up to the time of this study.

The pregnancy outcomes among these treated patients were divided for study purposes into two groups (table 1):

Table 1.—Stillbirth ratio in outcomes of women treated for syphilis before pregnancy

Group	Total out- comes	Live births	Fatal out- comes	Fatality ratio per 1,000 live births
A. Woman not pregnant when treated. B. Woman trea*ed	263	253	10	1 39. 5
during an earlier pregnancy	78	72	6	1 83. 3
Total	341	325	16	49. 2

¹ Difference between these ratios not statistically significant.

Group A—263 outcomes of pregnancy among those mothers who were not pregnant when treated. There were 253 live births and 10 fatalities (abortions, miscarriages. stillbirths. and deaths) in this group.

Group B-78 outcomes of pregnancy among those mothers who had received treatment during an earlier pregnancy. There were 72 live births and 6 fatalities in this group.

Only one autopsy was performed among the fatal outcomes of pregnancy, and this autopsy (on a stillbirth) showed that death was not due to syphilis. The

of syphilis in pregnancy. J. Ven. Dis. Inform.,

30:95-100, April 1949.

¹ Department of Dermatology and Syphilology of Western Reserve Medical School and of the Cleveland City and University Hospitals, in cooperation with John Rauschkolb, M. D.,

and Gerard DeOreo, M. D. ² Venereal Disease Control Officer, Chicago

Board of Health. ³ Director. Rapid Treatment Center, Belle-

vue Hospital, New York City. 4 Biostatistician, Division of Venereal Dis-

ease, U. S. Public Health Service. ⁵ Cole, H. N.; Plotke, F.; Thomas, E. W.; Jenkins, K. H.: Penicillin in the treatment

presence or absence of syphilis was not determined in the other 15 fatalities. Nevertheless, this fatality rate of 49.2 per 1,000 live births is probably lower than a comparable rate for the general population. For example, in New York City, where all results of pregnancy are required to be reported, the stillbirth rate in 1944 was 80.9 per 1,000 live births. Thus, it seems safe to assume that most of the 16 fatalities in this study were not due to syphilis.

For evaluation purposes, the results of pregnancy in these previously treated patients were classified according to clinical and serologic status, as follows:

- 1. Confirmed nonsyphilitic outcomes: live births with negative serologic results after at least 90 days of life or after autopsy that showed no evidence of syphilis.
- 2. Confirmed syphilitic outcomes: those outcomes of pregnancy in which a diagnosis of syphilis was established by clinical and serologic evidence.
- 3. Unconfirmed outcomes of pregnancy: those whose status could not be established, including fatal outcomes or neonatal deaths on which no autopsy was performed.

On the basis of these criteria, the status could be established in 229 of the outcomes of pregnancy: 193 of them from group A and 36 from group B (table 2). In each group, slightly more than 50 per-

Table 2.—Extent of syphilis among confirmed outcomes of women treated for syphilis before pregnancy

		l out- mes		hilitic comes	Nonsyph- ilitic outcomes	
Group	Number	Percent	Number	Percent	Number	Percent
A. Woman not pregnant when treated. B. Woman treated during an ear-	193	100.0	1	0. 5	192	99. 5
lier pregnancy Total	36 229	100.0	$-\frac{0}{1}$	0.0	36 228	99, 6

cent of these outcomes were from mothers who received less than 2,400,000 units of penicillin.

In group A (in which the mother was not pregnant when treated) the serologic status of the mother at time of delivery was negative in 161 cases, positive in 28, and unknown in 4. All the positive titers were 4 Kahn units or less, except in 3 mothers who exhibited 20 to 40 Kahn units at delivery.

Serologic tests on two infants in group A, both from mothers with positive tests at delivery, were positive at some time following birth. One infant had positive tests reported at 33, 47, and 68 days following birth, with subsequent negative tests at 95, 123, and 179 days, and was diagnosed as nonsyphilitic in the absence of symptoms of congenital infection. The mother of this child had a titer of less than 4 Kahn units at time of delivery. The second infant is the only one in this study in whom syphilitic infection could be attributed to failure of treatment administered to the mother. A detailed report of the case follows.

A Negro female, 22 years of age on admission, was treated for secondary syphilis in November 1944 (pretreatment titer, 160 Kahn units). She received 1,200,000 units of penicillin, became pregnant several months after treatment, and remained seropositive (40 to 80 Kahn units) during the entire pregnancy. The infant was born on October 3, 1945. There was no record of a serologic test being performed on the child until February 16, 1946, when the test was strongly positive. Congenital syphilis was diagnosed in the child, and treatment consisting of 2,000,000 units of penicillin was administered. In February 1946 the mother's blood had reached 160 Kahn units, and she was re-treated with 2.400,000 units of penicillin for serorelapse. Her blood was still positive (40 Kahn units) when she was last seen on August 30, 1946.

In group B (in which the mother was treated during an earlier pregnancy) the serologic status of the mother was known

to be negative at time of delivery in 29 cases, positive in 3 (1 case, 80 Kahn units; 2 cases, 4 Kahn units or less), and unknown in 4. Of these latter 7 pregnancies, 6 resulted in nonsyphilitic children, none of whom had a positive serologic test at any time following birth. The remaining pregnancy, in which the status of the mother's serologic test at time of delivery could not be definitely established, offers an interesting case history.

A Negro female, 23 years of age on admission, was treated for secondary syphilis (pretreatment titer, 120 Kahn units) in July 1945 during her fifth month of pregnancy. She received 1,200,000 units of penicillin with 360 mg. of arsenoxide. She attained seronegativity in October 1945 and gave birth to a nonsyphilitic child in November 1945. The mother maintained seronegativity as long as observed during a subsequent pregnancy; the last negative test prior to delivery was reported on October 28, 1946. The second child was born on November 16, 1946. On November 25 the mother had secondary lesions and a positive serologic test (32 Kahn units), and was diagnosed and re-treated as a probable reinfection. Negative serologic tests (Mazzini) were reported for the child on December 30, 1946, and on January 1, 1947. However, an X-ray of long bones revealed abnormalities suggesting congenital syphilis. the serologic test became positive, and on January 15 the child died with syphilis as a contributory cause. There is little doubt that the infection in the child was due to the new infection acquired by the mother late in pregnancy and could not be attributed to the inadequacy of the treatment administered during the initial infection. This outcome well illustrates the oft-repeated advice that all pregnant women should have at least two serologic examinations for syphilis during the course of pregnancy—once early in the pregnancy and again in the third trimester.

Summary

- 1. One case of congenital syphilis, representing a treatment-failure incidence of 0.4 percent of the 229 outcomes in which the status was established, indicates that no great likelihood of danger exists for a child born of a mother who has had satisfactory results to treatment for syphilis before she became pregnant, provided the woman has not relapsed during pregnancy. Further treatment may be withheld, but the patient should be kept under observation for evidences of failure.
- 2. No particular differences in results to treatment were found between women not pregnant when treated and those treated during a previous pregnancy.

The Patient's Attitude Toward Venereal Disease Education ¹

C. W. Buck, M. D., and G. E. Hobbs, B. A., M. D., M. P. R.

Introduction

Venereal disease education has been included in the public health programs of many countries in which concerted efforts are being made to reduce the incidence of venereal infections.

Controversy exists not only as to the form such education should assume, but also, and more fundamentally, as to the actual objective of venereal disease education. Should it serve primarily to teach the recently infected individual to seek diagnosis and treatment, or should it aim to modify sexual promiscuity?

It was felt that for clarification of some of these problems, it would be necessary to turn to the patients themselves, in order to learn what their experience with veneral disease education has been, in what way it has benefited them, and how they evaluate it in relation to other preventive measures.

Method of Survey

For this survey, the method of interview was selected. Over a period of 7 months (October 1948 to May 1949), 90 patients attending the venereal disease clinic at Victoria Hospital, London (Ont.), were interviewed.

Each patient was interviewed twice, except in a few instances wherein we knew that the patient could not be seen at the clinic again. At the first interview a general social history was taken, including age, sex, marital status, educational attainment, occupation, family background, residence, church affiliation, recreation, and use of alcohol. In the

To these data obtained from the patient was added a statement from the clinic nurse concerning the patient's regularity of attendance at the clinic for therapy and follow-up.

Method of Analyzing the Data

The analysis was designed to discover whether a relationship existed between (1) the patient's attitudes toward venereal disease; and (2) his social and educational background and his previous experience with venereal disease education. Comparison of all items obtained in the first interview with those obtained in the second interview was therefore necessary. To ascertain statistically wherein patients differed significantly in their attitudes toward venereal disease on the basis of differences in their background, use was made of the Chi-square test for goodness of fit.2 The copious statistical tables arising from this analysis have been omitted in the interest of brevity.

second interview the question of venereal disease was introduced, with a discussion of the patient's infection, the reason for his coming to the clinic, his experience with venereal disease education, his suggestions for personal protection against venereal disease and for general community prevention, and finally his opinions regarding the possible effects of venereal disease education. At the same time, a brief five-question test was given to the patient in order to determine roughly his knowledge of venereal disease.

¹ From the University of Western Ontario, London, Ont. This study was made possible by grants from the Ontario Department of Health and the Department of Education.

² The level of significance was taken as P <0.05, i. e., less than 5 chances in 100 that a difference could be ascribed to chance alone. In addition to presenting those findings which attained this level of significance, a few have been included which approached significance and appear to be worthy of mention.

Observations

Characteristics of Patients Studied

The characteristics of the patients and their venereal disease histories are given in detail in tables 1 and 2. These findings are similar to those of other studies of venereal disease clinic patients (1, 2). Because of the biased selection of patients in a free clinic, it is realized that such data throw no light on the background of venereal disease patients in the general population. In some respects, however, this group appears to be representative of the patients encountered in most out-patient clinics whether for venereal disease or other conditions.

Two other factors introduced a bias into the selection of patients: (1) the number of true marital contacts was deliberately limited because we felt that they did not constitute a real problem in venereal disease control; and (2) in the early stages of the survey, more patients

were interviewed in the morning clinic than in the evening clinic; since women are freer than men to attend the former, our group contains a higher proportion of women than would be expected if this were a truly unhiased sample.

The educational level of the patients, heing closely related to the problem under consideration, warrants special comment. Since the vast majority of the patients (78 out of 90) had completed less than 2 years of high school, this study draws its material primarily from people of lower educational attainment.

The patients fell into two groups of approximately equal numbers insofar as their contact with venereal disease education was concerned. One group had had no previous encounter with this type of education; the other group had had varying degrees of experience with different forms of venereal disease education. In some instances this experience had heen considerable, e. g., patients who had been

Table 1.—Characteristics of patients interviewed

Age in years: 15-19 20-29 30-39 40 and over	43 19	Family background: Home broken before age 15
Sex: Male Female	38 52	Grades 8-10 53 More than grade 10 7 Still at school 5
Marital status: Single Married Divorced or separated Widowed	$\begin{array}{ccc} 28 \\ 26 \end{array}$	Occupation: Unskilled laborer: City
Race: White Negro Indian	4	Domestic
Church affiliation: Protestant Roman Catholic None	13	High school
Childhood environment: RuralUrbanUndetermined	48	Excessive drinking 22 Social drinking 52 Abstinent 13 Undetermined 3

	Number of		Number of
Present infection:	patients		patients
Syphilis	59	Voluntary	40
Gonorrhea	31	Referral:	
		Contact	25
Source of infection;		Police	
Marital	7	Hospital	
Friend	44	Prenatal	6
Pick-up	34	Industry	
Unknown		Armed services	I
Chriowit	0	Children's aid	
Fraguerar of infactions		Ciliuren s ald	1
Frequency of infection:	70	A 4 4	
One infection			
More than one infection	18	Regular	
		Irregular	17
Source of venereal disease info	rma-		
tion:			
Hearsay	50		
Specific education			
	10		

exposed to the venereal disease education programs of the armed services; other patients had seen only general films presented during public campaigns against venereal disease.

Influence of Venereal Disease Education

Behavior.—If the circumstances surrounding the present infection are considered, there is no evidence that venereal disease education had any influence upon sexual behavior. For example, it was noted that infections derived from casual "pick-ups" were just as common in the group who had the advantage of venereal disease education as in those who did not. Furthermore, in the group of 18 patients with repeated venereal infections, all but 1 of these individuals had received venereal disease education before acquiring the second infection. We realize, of course, that in dealing with infected individuals, we have no way of knowing how many other persons were favorably influenced by education. The failures only are seen in a clinic.

There is evidence, however, that venereal disease education did influence behavior in seeking treatment; as a group, those who had received education tended to come to the clinic voluntarily upon suspecting the presence of infection.

Knowledge of venereal discase.—All patients were given a simple verbal test, covering the elementary aspects of syphilis and gonorrhea. These questions concerned methods of transmission, diagnosis, types of infection, occurrence of congenital infections, and reasons for instituting early treatment. Very few patients understood the factors involved in congenital infections, and many tended to regard the blood test as diagnostic for both syphilis and gonorrhea.

As was anticipated, factual knowledge was related principally to two factors:
(1) Those who had been exposed to venereal disease education, at even the most superficial level, were markedly superior in their understanding of the subject; and (2) a positive relationship existed between degree of occupational skill and level of general education, on the one hand, and knowledge of venereal disease, on the other.

Among patients who had received venereal disease education, those who gave written material as their source of information were definitely better informed. This was not thought to indicate the superiority of this medium of instruction, but rather that these individuals took the trouble to read about a subject in which they were genuinely interested.

It is interesting to note that as a group, patients reared in a rural environment had better knowledge of venereal disease than those from an urban setting. Most patients in the rural group had fair or excellent scores on the venereal disease information test, while poor, fair, and excellent scores were more evenly distributed in the urban group. It is difficult to account for this finding, since no significant difference was demonstrated between the two groups either in general educational level or in experience with venereal disease education.

Attitude toward venereal disease prevention.—The patients in this study fell into two groups of approximately equal numbers according to their ideas about venereal disease prevention and education.

1. One group accepted promiscuity as an established fact, and while admitting that venereal disease education might conceivably influence sexual behavior if given during childhood, they believed the only preventive procedure worthy of consideration at the adult level to be that involving direct control measures, such as blood testing, contact tracing, policing of hotels and restaurants, and increase in treatment and prophylactic facilities. This group felt that education should serve only as a method for bringing people into clinics for treatment. patients, as a group, showed poor knowledge of venereal disease, were heavy drinkers, had come, in a high proportion, from broken homes, had received minimal edúcation, and were irregular in clinic attendance. They could be described as persons of limited intellectual background, who came from a disturbed environment, and who had little concept of social welfare. Promiscuity was simply one aspect of their way of life. Although we would certainly consider these individuals in no position to formulate programs of prevention, we believe that any approach other than that suggested by them would have little success with their group.

2. The other group of patients felt that indirect methods aimed at the prevention

of promiscuity, through venereal disease education, control of alcohol, and provision of adequate community activities for young people, would be most effective. They thought in terms of influencing sexual behavior through adult education as well as through childhood training. In contrast to the first group, these patients had reached a higher educational level and had tended to come from more stable homes. They showed a much better factual knowledge of venereal disease, were social drinkers or abstainers, and were regular in clinic attendance. From a cultural and educational standpoint, they were closer to those whose duty it is to devise programs for the control of venereal disease.

Conclusions

Venereal disease education merits a place in preventive programs if only by virtue of its role in enabling the infected individual to seek treatment voluntarily. This survey indicates that for a certain element of the population, additional benefits are derived from education which are on an abstract rather than a concrete It has been seen that while the educated patient may know more about venereal disease and may have a better understanding of the problems of prevention, his sexual behavior may have not in itself been affected. The patients themselves pointed out that the time for most effective antipromiscuity education is in childhood training rather than in adult venereal disease education. By the time adulthood is reached, patterns of behavior are fairly rigidly established.

The over-all aim of venereal disease education should be, therefore, to provide simple but accurate information concerning the venereal diseases, stressing the means of achieving early diagnosis and treatment, the advantages and pitfalls of prophylaxis, and the prevention of congenital syphilitic infections. The subject of promiscuity might best be included in the discussion of transmission of infection, bringing out the direct relationship between number of sexual con-

tacts and chances of acquiring a venereal infection. In other words, the individual who is sexually intimate with 10 partners has many times the probability of acquiring an infection than has the person who is intimate with only 1 partner. Such an approach, although obvious, might influence the thinking of this group. The fact that degrees of promiscuity exist may well be recognized.

This survey suggests that because of differences in personality and social background, individuals differ in their attitudes to the venereal disease problem. Some are concerned purely with protection from or therapy for infection, assuming that sexual behavior will not be modified; others give consideration to the desirability of reducing promiscuity. This statistical analysis does not indicate, of course, that the two groups of individuals have differed in their sexual behavior, although differences between the two groups in clinic cooperation are shown.

Do these findings have any practical application to the planning of educational programs? Educational material designed for rather specific elements of the

population might be adjusted to fit the character of the group insofar as it is possible to distinguish those individuals who would be receptive to discussions of promiscuity from those who would not. Educational material offered at venereal disease clinics, for example, could be presented at two such levels.

Acknowledgment

The writers wish to express their gratitude to Dr. G. B. Sexton, director of the Venereal Disease Clinic at Victoria Hospital, London, Ont., and to Miss M. Best, the clinic nurse, for their cooperation in arranging interviews with the patients, as well as to Mr. J. R. Smiley, of the University of Western Ontario, for his assistance with the statistical analysis.

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The Identity of *Neisseria* Other Than the Gonococcus Isolated From the Genito-Urinary Tract¹

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In a previous paper (1) the author reported the frequent isolation of *Neisseria* other than the gonococcus from the genito-urinary tract; no effort to identify these organisms specifically was made, however. In the present series, additional sugars and biochemical tests were added for the purpose of identification.

Methods and Materials

Isolations were accomplished on the new 24-hour Difco medium (consisting of Bacto-GC medium base and Bacto-hemoglobin), in which 0.5 ml. to 1.0 ml. of Supplement B and 0.1 ml. of 2 percent tyrothricin per 100 ml. medium were used in place of Supplement A. A plate of this medium was inoculated directly by the attending physician, immediately upon obtaining the exudate from the patient.

Sugar broths for fermentation were

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prepared from Bacto-phenol red broth base, with 0.1 gm. of agar and 0.5 gm. of the desired Difco sugar added to each 100 ml. of the broth base.

For the determination of synthesis of polysaccharide from sucrose, pure cultures were grown on 1.5 percent Bactonutrient agar, containing 5 gm. Bactosucrose per 100 ml. of the agar. The test itself was performed by flooding the growth on the sucrose agar slants with Gram's iodine solution. Immediate blackening of the growth was taken to indicate polysaccharide synthesis.

Results

Biochemical reactions of the isolated strains studied are summarized in table 1. All reactions are those of newly isolated strains of oxidase-positive gramnegative diplococci. Patients were considered as having "recently" received penicillin if administered within a month previously.

Group I.—Three strains were isolated with the biochemical characteristics of Neisseria eatarrhalis (2, 3, 4): no visible acid was produced from any of the fermentable substances tested; no pigment was produced on Löffler's coagulate serum slant; and no polysaccharide synthesis from sucrose was noted. One of the strains was obtained from the vagina of a 3½-year-old Negro child who previously

had not received penicillin and who exhibited no symptoms of genito-urinary disease. The other two strains were from prostatic cultures obtained from two adult males between 20 and 30 years of age (one Negro and one white), of whom one had recently received penicillin and one had not. Neither revealed a purulent urethral discharge.

Group IIa.—Only one strain was isolated with the biochemical reactions of the meningococcus (2, 3, 4): visible acid was produced from dextrose and maltose only; a distinct yellow pigment was not produced on Löffler's medium; and polysaccharide synthesis was not observed. The strain was obtained from prostatic culture of a 36-year-old white male who recently had received penicillin. Since no mention was made of a urethral discharge, presumably there was none.

Group IIb.—Three strains were isolated with the biochemical characteristics of Neisseria subflava (2), Elser and Huntoon's chromogenic group III (3), and Gordon's chromogenic group 3 (4): acid was produced from dextrose and maltose only; and a definite yellow pigment was produced on Löffler's serum slant. The strains were obtained from the genito-urinary tract of two males and one female, all of whom had received recent penicillin therapy.

Group III.—Seven strains with the biochemical reactions of Neisseria flava (2),

Table 1.—Biochemical reactions of Neisseria other than the gonococcus isolated from the genito-urinary tract

	Biochemical reactions ¹					Löffler's serum slants		5-percent sucrose agar			
Group	Num- ber of strains	Dex- trose	Mal- tose	Su- crose	d- Fruc- tose	Lac- tose	d- Manni- tol	Growth	Yellow pigment	Growth	Polysac- charide synthesis
I	3 1 3 7 25 12 1 1 1 1 2	O A A A A A O O O O	O A A A A O A A A A	O O O A A O O O A	O O O A A A O O A A A	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0	Yes _	No	Yes	No. No. ? No. Yes. Yes. No. No. No. Yes.

¹ A represents visible acid produced; O represents growth without visible production of acid.

Elser and Huntoon's chromogenic group II (3), and Gordon's chromogenic group 4 (4) were isolated: visible acid was produced from dextrose, maltose, and fructose only; a distinct yellow pigment was produced upon Löffler's medium; and polysaccharide synthesis from sucrose was not After 1 day's incubation, colonies were smooth and glistening, up to 1.5 mm. in diameter, convex, with entire edge, almost opaque, yellowish-gray, and After 2 days the colonies were slightly larger; in some the edge was slightly serrated and occasionally slightly adherent to the medium, although the center remained viscid. After 3 to 4 days of incubation, the surface of some of the colonies was slightly contoured, the other characteristics remaining essentially the same. Five of the strains were obtained from the prostate or urethra of adult males between 20 and 40 years of age (all white except one), two of whom had received recent penicillin treatment. one patient had a purulent urethral discharge, and this had failed to reveal intracellular gram-negative diplococci in a direct spread of the exudate. Two of the strains were obtained from the urethra and ccrvix of white females. One of these patients was 51 years of age and had received recent penicillin, with no recorded symptoms of venercal disease; the other was 33 years of age and had received no recent penicillin therapy, nor was a purulent genito-urinary discharge present.

Group IV.—Thirty-seven strains with the fermentation reactions of Neisseria sicca (2, 3, 4) were isolated: visible acid was produced in dextrose, maltose, sucrose, and fructose, but not in lactose or mannitol. Polysaccharide was synthe-Twelve strains prosized from sucrose. definite yellow pigment Löffler's serum slants and were therefore biochemically identical with Elser and Huntoon's chromogenic group I (3), Gordon's chromogenic group 5 (4), and probably De Bord's Neisscria fulva (5). Culturally, none of the 37 strains exhibited the classical rough colonies of N. sicca.

Colonies in 24 hours were smooth and glistening, convex, up to 4 mm, in diam-

eter, usually with entire edge, although occasionally slightly undulate, almost opaque, yellowish-gray or grayish-white, and butyraceous or viscid. After 2 days some colonies were raised with a central peak, the edges of some were serrated, the surfaces were sometimes slightly contoured, and the edges of some were slightly adherent to the medium. After 3 to 4 days a few colonies were slightly brittle, although otherwise unchanged.

All but 6 of the 37 strains were obtained from both white and Negro adult males, the majority of whom recently had received penicillin; 17 patients had no purulent discharge, while 1 patient had such a discharge from the urethra. Since no mention was made of symptoms in 13 cases, presumably there were none. 6 patients, the exudates were obtained from the urethra, whereas 25 strains were obtained from prostatic culture. Six cultures were obtained from the cervix and urethra of adult females (5 Negro and 1 white), of whom 4 had received penicillin recently. One patient was reported as having a purulent discharge, and one as not having such a discharge. In 4 cases, no mention of symptomatology was made.

Group V.—This miscellaneous group of 5 strains produced a definite yellow pigment upon Löffler's serum slants and failed to produce visible acid from dextrose. With the possible exception of group Va, which corresponds biochemically to Neisseria flavescens (2, 6), it is felt that these strains really belong to the other chromogenic groups—Vb to IIb, Vc to III, and Vd to IV. Vd corresponds to the reactions of eight strains isolated by Cameron (6) and two strains isolated by Martin (7).

Discussion

The most frequently isolated *Ncisscria* other than the gonococcus belonged to group IV (table 1). Bergey (2) lists only two aerobic *Neisscria* species fermenting sucrose; namely, *sicca* and *pcrflava*. The former is described as being rough, nonpigmented, and failing to ferment mannitol. The latter is described as being

smooth, yellow-pigmented, and fermenting mannitol. The author has not to date found a truly gram-negative diplococcus with flattened adjacent sides in genitourinary exudates which, when newly isolated, fermented either lactose or mannitol. Consequently, group IVb (table 1) cannot be identified as perflava even though a yellow pigment is produced. On the other hand, IVb does meet the description of Elser and Huntoon's chromogenic group I (3) and Gordon's chromogenic group 5 (4). Group IVa (table 1) corresponds to N. sicca biochemically It differs from group IVb (2, 3, 4).only in failing to produce a definite yellow pigment on Löffler's slants. Although Elser and Huntoon (3) refer to sicca colonies as being firm and almost impossible to break up with a loop, only two of his 329 Neisscria cultures fit this description. Martin (7) states that in the early stage, colonies of sicca are like those of catarrhalis, and it is only later that there is frequent development of a corrugated Wilson (8) described a large surface. variety of Neisseria colonies fermenting sucrose, with colony characteristics varying from smooth to rough. Topley and Wilson (9) state that sicca is apparently only a rough variant of the smooth nasopharyngeal cocci, having observed the formation of rough variants from smooth strains, such rough strains being indistinguishable from sicca. The author has observed the formation of a definite vellow pigment on one batch of Löffler's medium while pigment production remained uncertain on another batch; hence, he feels that pigment production alone cannot be used as a basis for separating group IV (table 1) into separate species. He believes the following to be members of the same species: IVa and IVb of this series (table 1); the nonpigmented and rough sicca (2, 3, 4, 7, 8, 9); Elser and Huntoon's chromogenic group I (3); Gordon's chromogenic group 5 (4); and De Bord's fulva (5). The characteristic which apparently distinguishes this species from the other aerobic Neisseria is its ability to utilize sucrose; it not only produces visible acid from sucrose but also synthesizes polysaccharide from it.

The Neisseria which occurs next in order of frequency is group III (table 1). This group corresponds to Bergey's N. flava (2), Elser and Huntoon's chromogenic group II (3), and Gordon's chromogenic group 4 (4). Colonially, it is similar to group IV (table 1), but is apparently always pigmented and unable to utilize sucrose. The author believes this group to be sufficiently distinct to deserve species status. However, further work may reveal that it is a sucrose-negative variant of group IV.

There can be no doubt that the meningococcus of both serologic groups I and II has been isolated from the genitourinary tract (1θ) . Branham (11) states that the meningococcus never produces a definite yellow pigment such as that produced by the pigmented group of Neisseria. However, Elser and Huntoon (3), Martin (7), and Topley and Wilson (9) describe yellowish meningococcus colonies. Atkin (12) compared Gordon's four serologic types of meningococci with the colonial morphology of well-isolated colonies kept for relatively long periods of time on thick trypagar plates. Colonially, the meningococci were divisible into two groups. Types I and III had essentially the same colonies, and although the colonies were sometimes yellowish or pinkish, production of a definite yellow pigment was not mentioned. Types II and IV were essentially the same colonially, and a definite yellow pigment became apparent as the colony aged. Consequently, serologic group I, i. e., types I and III, which is the usual cause of epidemic cerebrospinal meningitis, is evidently nonpigmented, whereas group II, a heterogeneous group usually isolated from sporadic cases and carriers, may be pigmented. Obviously there is no adequate biochemical differentiation of the Neisseria fermenting only dextrose and maltose. Colonially and serologically, group I meningococci form a relatively homogeneous and recognizable group. The relationship and classification of the other Neisseria fermenting dextrose and maltose only, which are pigmented and serologically heterogeneous, remain to be defined.

There are two *Neisseria* occurring rather infrequently in the genito-urinary tract which ferment none of the sugars and which fail to synthesize polysaccharide from sucrose. One is nonpigmented and undoubtedly *N. catarrhalis* (2, 3, 4), while the other is biochemically the same as Branham's flavescens (2) and the two yellow meningitis strains isolated by Cameron (6).

Not infrequently strains of *Neisseria* fail to produce visible acid in dextrose and sometimes other sugars. The literature often contains descriptions of such atypical fermenters (4, 6, 7). It is doubtful that such strains, e. g., Vb, Vc, and Vd of this series, can be considered as separate species; several dextrose-negative strains on primary isolation have subsequently fermented this sugar and then been assigned to their proper group.

The Neisseria other than the gonococcus which are most frequently isolated from the genito-urinary tract, groups III and IV (table 1), are not easily mistaken for the gonococcus colonially. The gonococcus colony in 18 to 24 hours may have a diameter up to 1 mm. (although more often about 0.5 mm. maximum), is convex (with smooth and glistening surface and entire edge), translucent, colorless, butyraceous or viscid, and nonadherent to the medium. After 2 days the diameter may be as great as 3.5 mm., although usually it is about 2.0 mm. maximum. Colonies may now be either convex or raised with a central peak; the edge may be entire, undulate, or lobate; the surface may be smooth or slightly contoured and glistening; and the colonies may be translucent and grayish or translucent with a more opaque grayish-white center, butyraceous or viscid, and rarely adherent to the medium. In 3 to 4 days the colonies are essentially the same, but in some the edge may be crenated. Furthermore, colonies with a deeply wrinkled but glistening surface may appear. In 5 to 6 days colony diameter may be as great as 5 mm. Some colonies may now be drier and slightly brittle, and in a few the edges may be slightly adherent to the medium. Contrast these colonies with the description given above for groups III and IV of this series. The latter may be distinguished from the gonococcus in 24 hours by size, opacity, and color, and later by their margin as well. Obviously it is usually impossible to differentiate these Neisseria with certainty after the colonies are darkened by the oxidase test reagent. The nonpigmented N. catarrhalis and meningitidis are not so readily distinguishable from the gonococcus colonially.

A urethral discharge may be present in male patients at the time Neisseria other than the gonococcus are isolated from the genito-urinary tract. However, patients of groups III and IV (table 1) are apparently more often asymptomatic. Only rarely is the discharge profusely purulent and likely to be mistaken for an acute gonococcal infection; in no case may it be said with certainty that the nonspecific Neisseria isolated are responsible for the urethritis present. However, these nonspecific Neisseria may possibly have some degree of pathogenicity for the genito-urinary tract. Although their presence in this tract appears to be transient in most patients, they are occasionally isolated from two or more consecutive cultures taken at weekly intervals. Too few cultures of eatarrhalis and the meningococcus have been isolated to make any statements at present regarding their possible pathogenicity for the genito-urinary tract. Furthermore, since the clinical picture in the female is not clear, no observations may be made regarding the pathogenicity of the nonspecific Neisseria for the female genitourinary tract.

Summary

Neisseria with the biochemical characteristics of all the accepted aerobic species except N. perflava have been isolated from the genito-urinary tract. By far the commonest Neisseria other than the gonococcus which was isolated was one with the fermentation reactions of N. sieca, but which frequently produced a

greenish-yellow pigment on Löffler's coagulated serum and whose growth on 5-percent sucrose agar turned black when flooded with Gram's iodine solution. Colonies were observed to be smooth to intermediate and never truly rough on the new Difco chocolate-blood agar medium.

The next most frequently isolated *Neisseria* other than the gonococcus was *N. flava*. Both these organisms could usually be distinguished colonially from the gonococcus in 24 hours on the basis of colony size, opacity, and color, and later by the colony edge as well. Male patients from whom these two *Neisseria* were isolated were usually asymptomatic, although occasionally a watery or mucoid (rarely a purulent) urethral discharge was present.

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CURRENT LITERATURE

ACTA PATH. ET MICROBIOL. SCANDINAV., COPENHAGEN

On the diagnosis of lymphogranuloma venereum by means of Lygranum S. T. and Lygranum C. F. Tage Fløystrup, Flemming Reymann, and Alice Reyn. Acta path. et microbiol. Scandinav., 27: 94–106, Fasc. 1, 1950.

An account is given of the occurrence of positive Frei reactions and positive complement-fixation tests with Lygranum antigen (Squibb). The conclusion reached is that the Frei reaction with Lygranum antigen seems to be as specific in Denmark as can be expected in venereal disease patients.

AM. HEART J., St. Louis

Rupture of aortic aneurysm into the superior vena cava. Morris Alex. Am. Heart J., 39: 455-464, Mar. 1950.

The two cases reported bring the total to 104. Included is a review of the incidence, etiology, pathology, and physiology.

Syphilitic aneurysm of the aorta with rupture into the pulmonary artery. Arthur Klein and William B. Porter. Am. Heart J., 39: 465-472, Mar. 1950.

The patient, a 40-year-old white male, survived for 14 months after the onset of symptoms. Catheterization of the right auricle and ventricle was considered an important diagnostic aid for this patient.

AM. J. DIS. CHILD., CHICAGO

Pediatric proctology. Review with comment. Robert Turell. Progress in Pediatrics. Am. J. Dis. Child., 79: 510-538, Mar. 1950.

In this review the theories and developments as they have appeared in the literature are concentrated upon, one section being devoted to the venereal diseases: venereal lymphogranulomata and anorectal gonorrhea.

Quantitative and qualitative blood tests in treatment of congenital syphilis by penicillin. E. Dechene. Society Transactions. Am. J. Dis. Child., 79: 941, May 1950.

Five children, from 2 to 5 years of age, with congenital syphilis were treated with doses of 70,000 Oxford units penicillin G to each pound (0.5 kg.) of body weight. Monthly tests disclosed quantitative and qualitative modifications of serologic reactions for 1 year. Negative modifications were slower to appear than if arsenic or bismuth had been added, but the disease has been favorably modified.

AM. J. M. Sc., PHILADELPHIA

Angiocardiography in the diagnosis of cardiovascular syphilis. George E. Peabody, George G. Reader, Charles T. Dotter, Israel Steinberg, and Bruce Webster. Am. J. M. Sc., 219: 242-248, Mar. 1950.

At the New York Hospital 93 patients, 83 of whom were suffering from late syphilis, were studied as to merits of physical findings, conventional chest X-ray, and angiocardiography alone. A diagnosis of cardiovascular syphilis was effected in 15, excluded in 9, and sustained in 17 in which chest X-ray was negative.

The present status of penicillin in the treatment of syphilis in pregnancy and infantile congenital syphilis. Norman R. Ingraham, Jr., and Herman Beerman. Progress of Medical Science. Am. J. M. Sc., 219: 433-442, Apr. 1950.

This statement, prepared initially for presentation before the WHO Expert Committee on Venereal Infections, brings up to date previously published material and supplies a review of the current literature.

Aureomycin. Wallace E. Herrell. Therapeutics. Am. J. M. Sc., 219: 570-580, May 1950. The literature is extensively reviewed with particuar reference to the absorption, diffusion, and excretion of the drug, in vitro and in vivo activity, methods of administration and dosage, clinical studies, and toxicity.

AM. J. OBST. & GYNEC., ST. LOUIS

Cyclic changes in vaginal populations of experimentally induced *Trichomonas vaginalis* infections in Rhesus monkeys. Garth Johnson, Alfred B. Kupferberg, and Carl G. Hartman. Am. J. Obst. & Gynec., 59: 689-692, Mar. 1950.

When not accompanied by the objective signs of vaginitis observed in humans during the midcycle, the parasites are often difficult to demonstrate for prolonged periods in monkeys. There are no experimental data to explain this.

Penicillin therapy of the syphilitic pregnant woman: its practical application to a large urban obstetrical service. Virgene S. Wammock, O. M. Carrozzino, Norman R. Ingraham, and Nellie E. Clair. Am. J. Obst. & Gynec., 59: 806-819, Apr. 1950.

A report is presented of 820 pregnancies of syphilitic women at Philadelphia General Hospital from January 1, 1945, to March 31, 1948. A control of 5,596 non-syphilitic pregnancies is included. Arsenic and bismuth therapy resulted in 93.8 percent full-term normal and 2 percent living syphilitic infants. Penicillin therapy resulted in 94.5 percent normal full-term and 1.7 percent living syphilitic infants.

AM. J. OPHTH., CHICAGO

Clinical management of ocular syphilis. Brittain F. Payne, Jacob A. Goldberg, and John T. Simonton. Am. J. Ophth., 33: 605-610, Apr. 1950.

A survey is given, showing that ocular syphilis, although not as prevalent as formerly, is, when present, just as vicious as ever. The authors suggest that clinics and hospitals treat such cases in accordance with the newer therapeutic developments.

AM. J. ROENTGENOL., SPRINGFIELD

Calcification as a diagnostic sign of syphilitic aortitis. Editorials. Am. J. Roentgenol., 63: 414–416, Mar. 1950.

AM. J. ROENTGENOL, SPRINGFIELD-Con.

Findings from a review of the literature show that linear calcification of the ascending aorta in patients under 60 years of age is due to syphilitic aortitis in most cases. When calcification is found in this location, a diagnosis of syphilitic aortitis may be justified even with negative serologic findings.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

Studies on treponemal immobilizing antibodies in syphilis. II. Incidence in serum and cerebrospinal fluid in human beings and absence in "biologic false positive" reactors. Robert A. Nelson, Jr., Harold E. C. Zheutlin, Judith A. Diesendruck, and Perry G. M. Austin, Jr. Am. J. Syph., Gonor. & Ven. Dis., 34: 101–121, Mar. 1950.

Serums and cerebrospinal fluids from patients in various clinical categories were examined at Johns Hopkins Hospital. No positive reactions were obtained with serums from normal individuals or those with diseases other than syphilis. Strongly positive immobilizing activity was manifest in all serums from patients with syphilis beyond the primary stage. Serums from 12 patients with presumed biologic false-positive reactions were free of immobilizing antibody.

Studies on the life cycles of spirochetes. I.

The use of phase contrast microscopy.
Edward D. DeLamater, Victor D. Newcomer, Merle Haanes, and Richter H. Wiggall. Am. J. Syph., Gonor. & Ven. Dis., 34: 122-125, Mar. 1950.

Purpose of paper was to demonstrate usefulness of the phase contrast microscope of Zernicke in the study of spirochetes. Photographs made when this instrument is used afford excellent means for adequate documentation of observations. Photographs are given demonstrating stages in the cycle of the Nichols nonpathogenic test tube strain of spirochete.

Report of 726 patients who were re-treated following penicillin therapy for early syphilis. Evan W. Thomas and Simeon Landy. Am. J. Syph., Gonor. & Ven. Dis., 34: 126-143, Mar. 1950.

Data are given on 689 patients retreated for relapse or reinfection, 36 retreated for seroresistance, and 1 retreated for asymptomatic neurosyphilis during period from December 1943 to October 1947. Analyses are given of patients re-treated following original treatment of varying schedules. All patients were treated at Bellevue Hospital, New York City.

A study of syphilis and sexual habits in Greenland. Poul V. Marcussen and Joergen Rendal. Am. J. Syph., Gonor. & Ven. Dis., 34: 144-152, Mar. 1950.

The development of an epidemic at Frederiksdal in South Greenland and the measures taken to combat it are described.

Prolonged fever produced with three injections of typhoid vaccine. Ray O. Noojin, Bedford F. Pace, and Hugh B. Praytor. Am. J. Syph., Gonor. & Ven. Dis., 34:153-160, Mar. 1950.

Results in hours of fever produced were compared at the Medical College of Alabama in Birmingham with 36 patients who received therapy by means of two daily intravenous injections of typhoid vaccine and 20 patients given three daily injections. Three-injection technic produced prolonged temperature elevation and did not provoke abnormal risks or excessive expense. All patients had either neurosyphilis or some form of ocular syphilis.

Penicillin and fever therapy in early syphilis. A report of 161 patients treated with 2.4 million units of penicillin and physically induced fever. Frederick Plotke, George X. Schwemlein, Robert M. Craig, and Jack Rodriquez. Am. J. Syph., Gonor. & Ven. Dis., 34: 161-166, Mar. 1950.

Between July 1945 and May 1946, 148 patients were treated at the Chicago Rapid Treatment Center with sodium penicillin in aqueous medium intramuscularly every 3 hours for 7½ days, plus 3-hour sessions of artificial fever at 106° F. (rectal) on alternate days. Treatment for 13 additional patients was discontinued because of reactions. Results, shown in graph form, show that addition of fever increases effectiveness of penicillin therapy schedules.

AM. J. SYPH., GONOR, & VEN. DIS., ST. LOUIS—Continued

Experimental mouse syphilis. III. Bioassay of sodium penicillin and of penicillins X and G by a mouse-rabbit technique. Paul D. Rosahn and Catharine L. Rowe. Am. J. Syph., Gonor. & Ven. Dis., 34:167–176, Mar. 1950.

The method described utilizes the syphilitic mouse for therapeutic trial and the rabbit to determine the suppressive effect of the drug on the mouse infection. Crystalline penicillin G was 3 times as effective in suppressing infection as sodium penicillin, and 20 times that of crystalline penicillin X. The effective dosage is inversely related to complexity of the disease, with the mouse requiring the most and man the least.

Fatal hemoglobinuric nephrosis following intrathecal penicillin in neurosyphilis. A case report. V. Moragues and J. P. Wyatt. Am. J. Syph., Gonor. & Ven. Dis., 34: 177–181, Mar. 1950.

Patient was a 50-year-old woman. Death was attributed to sudden onset of hemoglobinemia and hemoglobinuria with the episode of shock and sequels following a second intrathecal administration of penicillin.

Tuberculoid gumma (Berdal), a rare type of syphiloderm. Report of a case. Frederick Rehm Schmidt, Roberto Jaramillo, and Antonio Donghi. Am. J. Syph., Gonor. & Ven. Dis., 34: 182–184, Mar. 1950.

Patient was a 34-year-old male successfully treated with pyrotherapy in conjunction with penicillin and an arsenical and bismuth preparation.

Treatment of gonorrhea with dihydrostreptomycin. Adolph Jacoby, William Goldberg, Nathan Sobel, and Theodore Rosenthal. Am. J. Syph., Gonor. & Ven. Dis., 34: 185-186, Mar. 1950.

Results of a study made by Department of Health, New York City, indicate that dihydrostreptomycin is a successful therapeutic agent. Eliminating 15 lost from observation in a group of 81 patients receiving a single injection of 0.5 gm., there was a 90.9-percent cure. Eliminating 21 lost from observation in a group of 94 receiving 1 gm., there was a 97.3-percent cure.

Oral penicillin in the treatment of gonorrhea. Raymond C. V. Robinson. Am. J. Syph., Gonor. & Ven. Dis., 34: 187-188, Mar. 1950.

In a study conducted at Johns Hopkins Hospital, a single oral dose of 250,000 units did not prove as effective as 75,000 units of procaine penicillin in oil given parenterally; however, 500,000 units orally produced similar results.

Experimental transfer of chemoresistant granuloma inguinale. Robert B. Dienst, Robert B. Greenblatt, and Calvin H. Chen. Am. J. Syph., Gonor. & Ven. Dis., 34: 189–190, Mar. 1950.

Subcutaneous transplantation of disease tissue from a known streptomycinresistant patient was made. Granuloma ulcer developed and proved to be streptomycin resistant. Both donor and recipient were cured with oral administration of aureomycin.

AM. PRACT., PHILADELPHIA

A new method for the intermittent injection of antibiotics. Bernard M. Wagner and Alexander E. Pearce. Am. Pract., 1: 58–60, Jan. 1950.

A study is reported in which the new multidose injector, a practical and easy instrument to use in the treatment of severe infections, was used for penicillin and streptomycin injections. This injector greatly lessens the need for services of nurses or other trained personnel.

ARCH. DERMAT. & SYPH., CHICAGO

Lymphoblastoma cutis. Report of a case treated with nitrogen mustard. A. M. Brixey, Jr., and John H. Lamb. Arch. Dermat. & Syph., 61: 800-812, May 1950.

Case history is presented of a 45-yearold Negro male who developed lymphoblastomatous involvement of skin, lymph nodes, and blood following treatment of syphilis with arsenicals.

ARCH. OPHTH., CHICAGO

Early diagnosis of syphilitic primary optic nerve atrophy. Joseph V. Klauder and George P. Meyer. Arch. Ophth., 43: 537– 552, Mar. 1950.

By using data on patients treated at Wills Hospital, Philadelphia, the authors

ARCH. OPHTH.. CHICAGO—Continued discuss the earliest signs of atrophy and the pitfalls in early diagnosis. Most frequent prodromal symptoms other than impaired visual acuity were pain in the legs and diplopia. Pathology and early ophthalmologic diagnosis are discussed. Case histories of seven patients are presented.

Biochem. J., London

The site of action of penicillin. 1. Uptake of penicillin on bacteria. D. Rowley, P. D. Cooper, P. W. Roberts, and E. Lester Smith. Biochem. J., 46: 157–161, Feb. 1950.

The preparation of radioactive penicillin used in these studies is described. The amount of penicillin which becomes attached to bacteria under various conditions was measured, and the uptake most likely responsible for its antibacterial activity was distinguished. The authors believe that this uptake is due to a direct chemical reaction with a cellular component present in minute amounts in resting bacteria, more of which appears to be produced during growth.

BRAIN, LONDON

Delayed withdrawal reflex and perception of pain: Studies in a case of syphilitic meningomyelitis and tabes with extensor plantar responses of a type not previously described. Michael Ashby. Brain, 72: 599-612, Dec. 1949.

A detailed case report of this patient is presented. Clinical methods of study and results are reported. The literature is reviewed and discussed.

Brit. J. Ven. Dis., London

Some individual and social factors in veneral disease. Robert Sutherland. Brit. J. Ven. Dis., 26: 1-15. Mar. 1950.

A review of the literature is given in a discussion which includes the incidence of venereal disease and promiscuity. Since promiscuity is the fundamental problem found in examining the individual and social factors in venereal disease, it is discussed as to age of patients, sex,

intelligence, education, religion, marital status, socioeconomic status, family background, personality, alcohol, effects of war, and reasons for promiscuity.

Laboratory examinations for gonococcal infection in the female. K. E. Cooper, A. Mayr-Harting, and A. E. W. McLachlan, Brit. J. Ven. Dis., 26: 16–22, Mar. 1950. The limitations of smears, accuracy of

The limitations of smears, accuracy of cultures, and gonococcal complement-fixation tests are discussed.

Oral penicillin in the treatment of gonococcal urethritis. G. O. Horne. Brit. J. Ven. Dis., 26: 23-28, Mar. 1950.

An effective treatment using oral penicillin tablets, each containing 100,000 units of calcium penicillin buffered with sedium citrate, given in 2 doses of 5 tablets each, at intervals of 3 to 6 hours, is described as a result of experience with 50 patients. In only 1 patient was adjuvant treatment required.

A vegetable extract used as an antigen for the Kahn test: an experimental trial. John S. Stevenson. Brit. J. Ven. Dis., 26: 29-30, Mar. 1950.

An extract of soya bean flour was substituted for the antigen of the standard Kahn test. When fresh it reacted strongly with 80 percent of the positive serums tested. When 4 weeks old, it produced unreliable results. Findings indicate reason why vegetable antigens in general are unsuitable for use in serologic tests.

Complement-fixation technique, II. The titration of Wassermann antigen. I. N. Orpwood Price. Brit. J. Ven. Dis., 26: 33-36, Mar. 1950.

Article describes technic of standardizing the Wassermann antigen.

BULL, JOHNS HOPKINS HOSP., BALTIMORE

The effect of the size of the inoculum (number of treponemes) upon the course of experimental syphilis in the rabbit. Richter H. Wiggall and Alan M. Chesney. Bull. Johns Hopkins Hosp., 86: 191-199, Apr. 1950.

This experiment done at Johns Hopkins University suggests that the size of inoculum has a direct effect upon the course of experimental syphilis when injected intravenously. In 45 rabbits receiving an Bull. Johns Hopkins Hosp., Baltimore—Continued

inoculum of 770,000 treponemes, 87 percent showed lesions, while in 42 receiving 7,700 treponemes, only 48 percent showed lesions. Lymph nodes were shown to be a more constant reservoir of syphilitic infection than the liver.

BULL. NEW YORK ACAD. MED., NEW YORK

The diagnosis of lymphogranuloma venereum with special reference to the complement fixation test. Norton M. Luger. Bull. New York Acad. Med., 26: 265, Apr. 1950.

The quantitative complement-fixation test is valid and specific for lymphogranuloma venereum as evidenced by 31 patients tested. Of these, 80 percent had titers of 1:20 or more on admission to the hospital, and by the end of the second week, 94 percent had titers of that magnitude.

CANAD. M. A. J., MONTREAL

The problem of specific therapy in cardiovascular syphilis. R. Roy Forsey. Canad. M. A. J., 62: 339-341, Apr. 1950.

The principles of treatment of cardiovascular syphilis before the advent of penicillin are reviewed. Cases reported in the literature which have been treated with penicillin are summarized. No conclusions can be drawn as yet concerning penicillin therapy of cardiovascular syphilis.

Reiter's syndrome. G. E. Ffrench and M. L. Mador. Canad. M. A. J., 62: 374-375, Apr. 1950.

A case report is presented of a 28-yearold white male with Reiter's syndrome. The literature is reviewed, and the authors find there is evidence that coitus plays a part, the nature of which is still uncertain.

CHRON. WORLD HEALTH ORGAN., GENEVA Fifth session of the Executive Board. Chron. World Health Organ., 4: 99-109, Apr. 1950.

At the meeting in Geneva in January 1950, the report of the Expert Committee on Venereal Infections was reviewed, and attention was directed to the epidemiologic aspects of control, particularly as related to seafarers. Full support was

given to the syphilis and yaws control projects in Haiti and to the bejel control project in the eastern Mediterranean region.

CIRCULATION, BALTIMORE

Catheterization of the left side of the heart in man. Henry A. Zimmerman, Roy W. Scott and Norman O. Becker. Circulation, 1: 357-359, Mar. 1950.

The technic employed is described in detail. The left ventricle was entered in 11 patients with syphilitic aortic insufficiency, with no untoward complications. Failure to pass the aortic valves in normal subjects is discussed.

Electrocardiographic changes in a case of left ventricular and septal hypertrophy resembling anterior myocardial infarction.

Aaron Burlamaqui Benchimol and Paul Schlesinger. Circulation, 1: 970-974, April 1950 (Part II).

A case history is presented of a 47-yearold Negro mechanic with syphilitic aortic insufficiency and marked left ventricular hypertrophy, in whom the electrocardiogram was extremely suggestive of anterior myocardial infarction, which was not found to be present at autopsy.

Electrokymographic studies in insufficiency of the aortic and pulmonic valves. Howard E. Heyer, Ernest Poulos, and Julian H. Acker. Circulation, 1: 1037-1048, Apr. 1950 (Part II).

At the Department of Internal Medicine, Southwestern Medical College, Dallas, Tex., electrokymographic studies of the heart and great vessels were made in 22 patients with clinical signs of aortic insufficiency. In 16 the origin was syphilitic and in 6 it was rheumatic. Alterations in the shape of the aortic ejection curve were found and were accompanied by a diminution or absence of the incisura. Alterations in heart border motion of the ventricles were also found.

DIS. NERV. SYSTEM, CHICAGO

Pyridoxine and thiamine therapy in disorders of the nervous system. Simon Stone. Dis. Nerv. System, 11: 131-138, May 1950.

In this study from the Neurological Service of Elliot Hospital, Manchester, N. H., New Hampshire State Hospital, and Crippled Children's Services of the DIS. NERV. SYSTEM, CHICAGO—Continued State of New Hampshire, intraspinal pyridoxine therapy alone or in combination with intraspinal thiamine was administered to 169 patients with a variety of nervous system disorders, including 38 with general paresis, 23 with tabes dorsalis and taboparesis, 4 with tabetic optic atrophy, and 2 with syphilitic spastic paraplegia. Favorable results were obtained in most cases, and no toxic manifestations were observed.

EDINBURGH M. J., EDINBURGH

G. P. I.: Its juvenile and senile types. R. M. Stewart. Edinburgh M. J., 57: 17–29, Jan. 1950.

In this general review the author discusses incidence, sex distribution, age at onset, duration, family history, symptomatology, clinical course, pathology, differential diagnosis, and treatment. Juvenile and senile types are differentiated. Case reports of two patients with senile general paralysis are presented.

GEORGIA'S HEALTH, HAPEVILLE

VD prevention lags. Georgia's Health, 30: 2, Mar. 1950.

Prevention lags not from treatment but from lack of education. Medicine cannot be substituted for morals. The prescription for prevention is intelligent sex instruction, a comfortable environment, and an example of happy married life on the part of parents.

HEALTH, TORONTO

Venereal disease—a challenge to industry. B. D. B. Layton. Health, pp. 15, 31, Mar.—Apr. 1950.

The author discusses the part played by industry in the fight against venereal diseases and presents reasons why industrialists should be vitally concerned in helping to eliminate them.

HEALTH NEWS, ALBANY

Preventive medicine in Sing Sing. Charles C. Sweet. Health News, 27: 3-5, 8-12, Jan. 1950.

One phase of preventive medicine described is that of syphilis. The prison has proved to be a valuable field for research

requiring prolonged observation. In cooperation with New York State Department of Health, more than 5,000 syphilis patients were treated and followed for as long as 10 years.

INDIAN J. VEN. DIS., BOMBAY

Cardiolipin antigens in the serodiagnosis of syphilis. Johs Kvittingen, John C. Cutler, and R. B. Tampi. Indian J. Ven. Dis., 16: 1-4, Jan.-Mar. 1950.

A review of the literature is presented. For the purpose of interchange of information on results of treatment, serologic surveys, etc., on an international scale, it is hoped that a standard test may be worked out by the Expert Committee on Venereal Infections.

Modern treatment of syphilis, Theodore Rosenthal. Indian J. Ven. Dis., 16: 5-10, Jan.-Mar. 1950,

A review of accepted definitions in various phases of syphilis is given as well as recommended treatments and criteria of cure.

J. A. M. A., CHICAGO

Terramycin in the treatment of venereal disease. A preliminary report. F. D. Hendricks, A. B. Greaves, S. Olansky, S. R. Taggart, C. N. Lewis, G. S. Landman, G. R. MacDonald, and Henry Welch. J. A. M. A., 143: 4-5, May 6, 1950.

At the Polk Health Center and the Rapid Treatment Center of Gallinger Hospital, Washington, D. C., 73 patients with gonorrhea, 6 with syphilis, and 2 with granuloma inguinale were treated. From 1 to 2 gm. of terramycin hydrochloride in divided doses gave a cure rate of 80 to 100 percent in gonorrhea patients. Clinical healing of lesions of syphilis occurred when the drug was given orally in doses of 60 mg. per kilogram of body weight per day for 8 days and of granuloma inguinale when the same amount was given for 12 days.

Venereal disease among Norwegian troops in Germany. J. A. M. A. 143: 195, May 13, 1950.

In five brigades stationed in Germany in rotation between February 1947 and August 1949, the syphilis rate was 14 per thousand, while in Norway during the same period, the rate for Army personnel

J. A. M. A., CHICAGO—Continued

was only 2 per thousand. Forty cases of latent syphilis were discovered in the troops on return to Norway. This tallies with the opinion that every fifth syphilitic male presents no clinical manifestations of early syphilis. Gonorrhea rates were also higher for troops stationed in Germany.

J. AM. M. WOMEN'S A., NASHVILLE

Vaginal infections. Katherine Kuder. J. Am. M. Women's A., 5: 173-179, May 1950.

The main types of specific vaginitis are those caused by the gonococcus organism, the parasitic fungus *Monilia*, and the parasite *Trichomonas vaginalis*. Each of these is discussed as to characteristics, mode of transmission, and therapy.

J. BIOL. CHEM., BALTIMORE

Biochemical studies on chloramphenicol (Chloromycetin). III. Isolation and identification of metabolic products in urine. Anthony J. Glazko, Wesley A. Dill, and Mildred C. Rebstock. J. Biol. Chem., 183: 679-691, Apr. 1950.

A study was made at the Parke Davis Company, Detroit, in which the drug was isolated from urine and identified. Hydrolysis products were identified by paper partition chromatography, by direct isolation of chloramphenicol, and by preparation of saccharic acid dibenzimidazole from glucuronic acid.

J. Iowa M. Soc., Des Moines

Strokes—their evaluation and treatment. Abe B. Baker. J. Iowa M. Soc., 40: 107-112, Mar. 1950.

Adequate treatment can be instituted only after the cause has been determined, Both general paresis and meningovascular syphilis are listed as causes of strokes, Every adult stroke patient should have a spinal fluid evaluation,

J. MAINE M. A., PORTLAND

Ophthalmoscopic diagnosis of importance to the medical man as seen in the retinal blood vessels. Edmund B. Spaeth. J. Maine M. A., 41: 34-39, Feb. 1950. The importance of ophthalmoscopic diagnosis in syphilis, tuberculosis, and cardiovascular-renal diseases is considered at length. Detailed descriptions are given of the pathologic processes of these diseases as manifested in the retina.

J. MICHIGAN M. Soc., LANSING

Diagnosis and treatment of anorectal diseases. Harry E. Bacon and Timothy F. Moran. J. Michigan M. Soc., 49: 309-314, Mar. 1950.

Conditions which characterize anorectal infections of lymphogranuloma venereum are discussed. A nutritious diet and local instillations of ichthyol (10 cc. of a 25-percent aqueous solution twice daily) are recommended for treatment to soothe the mucous membrane.

J. PEDIAT., ST. LOUIS

Natal and neonatal teeth. A review of twenty-four cases reported in the literature. Maury Massler and Bhim Sen Savara. J. Pediat., 36: 349-359, Mar. 1950.

Only one of these had a history of congenital syphilis, thus making it appear unlikely that congenital syphilis is causative in the premature eruption of teeth,

J. Roy. Army M. Corps, London

"One shot" treatment of venereal diseases employing procaine penicillin G with aluminum monostearate (P. A. M.). R. R. Willcox. J. Roy. Army M. Corps, 94: 126-134, Mar. 1950.

From experience gained during a survey in Southern Rhodesia, the author believes that the single-shot treatment will be of value in treating venereal diseases in native populations in places where a doctor can visit only once a week or less and where diagnostic facilities are minimal.

J. Social Hyg., New York

The armed forces and social hygiene. The character guidance program in action. Charles I. Carpenter. J. Social Hyg., 36: 87-91, Mar. 1950.

15

A description of the Air Force character guidance program includes the part played by the Special Service Office, Office of Information and Education, the Air

J. Soc:AL Hyg., New York—Continued Provost Marshal, the Surgeon, and the Chaplain.

The role of voluntary social hygiene agencies in the World Health Organization program to fight venereal diseases. John F. Mahoney. J. Social Hyg., 36: 92-95, Mar. 1950.

A discussion is presented of voluntary leadership at home and abroad and the world view. Points are listed upon which the foundation of a venereal disease control program is based.

J. SOUTH CAROLINA M. A., FLORENCE

Liver cirrhoses: a review. Douglas Symmers. J. South Carolina M. A., 46: 115–122, Apr. 1950.

A classification is presented of the various forms of liver cirrhoses, including the congenital and acquired syphilitic groups, together with a discussion of the incidence, symptomatology, anatomic picture, and treatment.

J. Urol., Baltimore

The histopathology of lymphogranuloma venereum. Edward B. Smith and R. Philip Custer. J. Urol., 63: 546-563, Mar. 1950.

A general description is given of the histopathologic changes seen in lymphogranuloma venereum, based on a study of 2 autopsies and 558 surgical specimens.

M. ANN. DISTRICT OF COLUMBIA, WASH-INGTON

Can penicillin conquer VD? William P. Herbst. M. Ann. District of Columbia, 19: 264-265, May 1950.

Medication can cure individual patients, but it can't coutrol venereal disease. Only education, ethical guidance, and character building can do that. Facts are presented which show progress being made in diagnosis and treatment.

M. J. AUSTRALIA, SYDNEY

Procaine penicillin; its effectiveness in maintaining blood levels, and its use in the treatment of general paralysis of the insane. Ian Martin. M. J. Australia, 1: 292-295, Mar. 4, 1950.

A review of the literature is presented along with a program of investigation into the value of penicillin. Two case histories are given which show value of treatment.

General paralysis of the insane treated with procaine penicillin. W. F. Salter. M. J. Australia, 1: 300, Mar. 4, 1950.

Case history is presented of a woman admitted to hospital in a confused and restless state. It was demonstrated that procaine penicillin injected three times a week maintained an adequate therapeutic blood level. Patient's excitement and confusion disappeared. Wassermann test remained positive.

NATURE, LONDON

Aureomycin in the treatment of yaws and tropical ulcer in Africa. O. Ampofo and G. M. Findlay. Letters to the Editors. Nature, 165: 398–399, Mar. 11, 1950.

Three African children with florid secondary yaws were given six capsules (250 mg. per capsule) of aureomycin daily for 7 days. By the seventh day the lesions had almost completely healed, but no serologic changes were noted 6 weeks after cessation of treatment. Four patients with tropical ulcers received aureomycin for 4 to 7 days, resulting in complete healing. Further observations are being undertaken.

QUART. BULL, DEPT. OF HEALTH, NEW YORK, NEW YORK

A look into the future. John F. Mahoney. Quart. Bull. Dept. of Health, New York. 18: 4-8. Spring 1950.

Future development in field of antibiotic research is of basic importance in the practical control of venereal disease. By curtailing opportunities for transmission, a progressive spiral of decline may be started in motion which will progress to a point at which the diseases may pass from the public health sphere.

S. CLIN. NORTH AMERICA, PHILADELPHIA

The present status of antibiotics and other agents for the treatment of urinary infections. Russell D. Herrold. S. Clin. North America, 30: 61-69, Feb. 1950.

The methods of administration of peni-

S. CLIN., NORTH AMERICA—Continued cillin, streptomycin, aureomycin, Chloromycetin, sulfonamides, and sulfones are reviewed, and the problem of bacterial resistance is considered. Treatment of various urinary infections, including gonococcic and *Trichomonas* infections, is discussed.

The differential diagnosis and treatment of vulvar lesions. M. Edward Davis. S. Clin. North America, 30: 267-286, Feb. 1950.

Among the various infections leading to vulvar lesions the author includes trichomoniasis, syphilis, condyloma acuminatum, granuloma inguinale, and lymphogranuloma venereum, with a discussion of symptomatology, diagnosis, and treatment.

SOUTH, M. J., BIRMINGHAM

A four-year study of penicillin treatment of syphilis of the central nervous system. J. Lamar Callaway, Arthur H. Flower, Jr., Victor R. Hirschmann, and Sidney Olansky. South. M. J., 43: 412–422, May 1950.

In this work done at Duke University School of Medicine, of 207 patients treated, 34.8 percent returned to nearnormal, 42 percent showed moderate improvement, while 23.2 percent received little or no benefit from therapy. Combined penicillin and fever therapy did not prove more effective than penicillin alone in a dosage of 4 to 6 million units. Patients with symptomatic paresis responded best while those with congenital central nervous system syphilis responded most poorly.

SOUTH. MED. & SURG., CHARLOTTE

Lessons from an unusual case of general paresis. Isaac C. East. South. Med. & Surg, 112: 35-36, Feb. 1950.

A case is reported of syphilitic meningoencephalitis (general paralysis) with manic features in a 36-year-old white man admitted to Eastern State Hospital, Virginia, on December 16, 1948. The first Wassermann was doubtful, but the second was positive. The patient is now receiving treatment consisting of 6,000,000 units crystalline procaine penicillin G in sesame

oil with 2 percent aluminum monostearate. This will be followed by malarial fever therapy. Prognosis is fair.

TODAY'S HEALTH, CHICAGO

The masquerader. Alpert P. Seltzer. To-day's Health, 28: 50-51, 60, Mar. 1950.

In this general review the author warns how syphilis can imitate and mimic almost any disease in internal medicine, thus acquiring the title "the masquerader."

U. S. NAV. M. NEWS LETT., WASHINGTON

BuMed circular letter 50–36, 17 April 1950. Venereal disease; use of oral penicillin as additional prophylaxis for prevention of. U. S. Nav. M. News Lett., 15:17–18, May 5, 1950.

National Research Council Subcommittee on Venereal Disease recommended to the Armed Forces the use of a single oral penicillin tablet (250,000 units) to be taken when the man first reports for prophylaxis after exposure. This measure replaces the chemical prophylaxis of gonorrhea.

UROL. & CUTAN. REV., WEST PALM BEACH

In vitro studies on the trichomonacidal effect of certain drugs and antibiotics. Robert B. Greenblatt and Robert M. West. Urol. & Cutan. Rev., 54: 72-77, Feb. 1950.

This article deals with the effect of various drugs and antibiotics alone and the synergistic effect of certain of these drugs and antibiotics when used in "in vitro" studies. Nineteen milligrams sulfathiazole and 1.5 milligrams of aureomycin in combination gave motility for only 5 minutes after start of test—so that one-fourth of the concentration of each drug was effective in only half the time interval. It seems that some combinations did not show synergistic effect while others showed marked enhancement.

Nonspecific urethritis successfully treated with Chloromycetin. Calvin H. Chen and Robert B. Dienst. Urol. & Cutan. Rev., 54: 77-79, Feb. 1950.

A detailed report is presented of a case of recurrent nonspecific urethritis successfully treated with Chloromycetin—in dosage of 1 gm. three times per day. The

UROL. & CUTAN. REV., WEST PALM BEACH—Continued

action of the drug is probably on a virus believed by the authors to be the most likely causative agent.

An improved method of reporting serologic tests in syphilis. D. Truett Gandy and W. A. Clark. Urol. & Cutan. Rev., 54: 82-85, Feb. 1950.

A new form is suggested featuring (a) a seal indicating a laboratory approved by a State board of health, (b) prompt reporting of statistical data for epidemiologic study, (c) suggestions to physicians for clinical application of the results of blood and spinal fluid examinations,

and (d) pertinent information for patients with early syphilis.

WEST. J. SURG., PORTLAND

Genital, extragenital and skeletal granuloma inguinale. Report of a case. Robert G. Lipp and Douglas E. Bibby. West. J. Surg., Portland, 58: 173-177, Apr. 1950.

A case is reported of osteomyelitis of the tibia and similar bilateral osteomyelitis of both radii, together with genital and soft tissue lesions, caused by granuloma inguinale in a 20-year-old colored female. Therapy consisted solely of bed rest and streptomyein.

STATISTICS

Reported Cases of Congenital Syphilis, Continental United States, Fiscal Year 1949

A. Percent distribution of all cases, by race and sex

Danamadan	Cases reported by all sources						
Race and sex	Number		Percent				
Total	14, 295		100.0				
White	9, 412	2, 071 2, 812 4, 225 5, 187	32. 2 65. 8	14. 5 19. 7 29. 5 36. 3			
MaleFemale	6, 2 96 7, 999		$\frac{44.0}{56.0}$				

B. Percentage of all cases reported by private physicians

Race and sex	Cases reported by all sources	Cases reporte	d by private icians
	Number	Number	Percent of all cases
Total	14, 295	3, 101	21. 7
White_ Male_ Female_ Nonwhite Male Female_ Female_	4, 883 2, 071 2, 812 9, 412 4, 225 5, 187	2, 317 854 1, 463 784 281 503	47. 4 41. 2 52. 0 8. 3 6. 6 9. 7
Male Female	6, 296 7, 999	1, 135 1, 966	18.0 24.6

Source: PHS Form 8958-B FSA-PHS—Division of Venereal Disease, Office of Statistics, 5/26/50 (EJD-MJB)-knc,



DOCUMENTS SECTION

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FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

FS2.9

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 15 cents. Subscription Price: Domestic \$1.25 a year; foreign \$2.00

Measurement of Trend of Syphilis in Mississippi

A. L. Gray, M. D., Lida J. Usilton, M. A., and Albert P. Iskrant, M. A.

In the operation of a health program to control syphilis, we are continuously faced with the evaluation of the program in terms of achieving its objective. do this, we study trends in the incidence and prevalence of the disease and trends in mortality, infant mortality, and insanity caused by the disease. When possible we also examine increases or decreases in illness or incapacity caused by syphilis. To estimate or measure trends in any particular factor we must have some objective data which can be used for that purpose. Following are some of the factors and the data used to estimate them for the trend of syphilis in Mississippi.

Mortality from Syphilis

The trend of mortality from syphilis in Mississippi is downward. Usually the mortality data tabulated from the cause of death given on the death certificate are used. It is realized that the recorded mortality rate from syphilis is synonymous with the actual mortality rate. Various studies show corded rate from syphilis to be lower than the true rate. It is believed, however, that there has been no tendency between 1938 and 1948 toward a decrease in the completeness of syphilis mortality reporting. Moreover, the method of coding the cause of death in the National Office of Vital Statistics also influences the recorded cause of death. This coding has been constant between 1939 (fifth revision) and 1948 (sixth revision). It is believed therefore that the downward trend in reported mortality does in fact reflect a reduction in the actual mortality rate. In like manner the downward trend in reported infant mortality due to syphilis is believed to reflect a decrease in the true rate (table 1).

Table 1.—General mortality due to syphilis, infant mortality due to syphilis, and first admissions to State hospitals with psychoses due to syphilis in Mississippi, 1933–48 ¹

	Mortality rate (per	First admissions to State	Infant mortality (per 1,000 live births 2)				
Year	100,000 popula- tion ²)	psychoses due to syphilis (per 100,000 population)	Total	White	Non- white		
1933_ 1934_ 1935_	20. 0 18. 3 18. 2	5. 9 4. 5 3. 7	1. 2 1. 1 . 9	0. 2 . 2 . 2	$\begin{array}{c} 2.1 \\ 2.0 \\ 1.5 \end{array}$		
1936_ 1937_ 1938_ 1939_ 1940_	17.7 23.9 24.5 24.2 21.6	6. 2 6. 3 3. 6 7. 9	1. 2 1. 7 1. 2 1. 4 1. 1	.2 .3 .3 .4 .2	2.1 2.8 1.9 2.2 1.8		
1941_ 1942_ 1943_ 1944_ 1945_	19. 7 19. 5 18. 0 14. 7 12. 6	3. 9 7. 1 7. 7 5. 2 6. 1	.9 .9 .6 .7	.2 .2 .1 .2	1. 6 1. 5 1. 0 1. 2 1. 1		
1946. 1947. 1948.	10.3 10.1 9.9	7. 0 5. 7 4. 6	.3 .2 .3	0 0 .1	.6		

¹ Sources: J. Vcn. Dis. Inform., 27: (face p. 238), October 1947. National Office of Vital Statistics, FSA (PHS): Special Reports, State Summaries, 1946, 1947; Births, Stillbirths, and Infant Mortality Statistics, 1937–1946; Unpublished General Mortality Due to Syphilis Rates, 1950; Unpublished Infant Mortality Due to Syphilis Rates, 1950. Bureau of the Census: Patients in Hospitals for Mental Diseases, 1933–1937, and Patients in Mental Institutions, 1938–1946; National Institution of Mental Health Special Release, 1947–1948.

¹ Director, Division of Preventable Disease Control, Mississippi State Board of Health. ² Director, Program Operations, Division of Venereal Disease, U. S. Public Health Service.

³ Principal Statistician, Division of Ve-

nereal Disease, U. S. Public Health Service.

² 1933–1940, by place of occurrence; 1941–1948, by place of residence.

³ Excluded because of incomplete reporting.

Note: Abstracting of clinic records and preliminary tabulation on prevalence were performed by Eloise T. Worden, B. S., Health Program Analyst, Division of Venereal Disease, U. S. Public Health Service.

⁴ International Statistical Classification of Diseases, Injuries, and Causes of Death, Vol. 1, 1948.

Insanity

The trend of the admission rate to State mental hospitals with psychoses due to syphilis has not been downward, nor has the proportion of all psychoses due to syphilis. One of the inconsistent facets of venereal disease control is the

Incidence

The true incidence ⁵ of syphilis in Mississippi is unknown but we believe that, within limits, morbidity reporting can be used to estimate trends in the incidence. Since morbidity reporting by private physicians is too variable to use

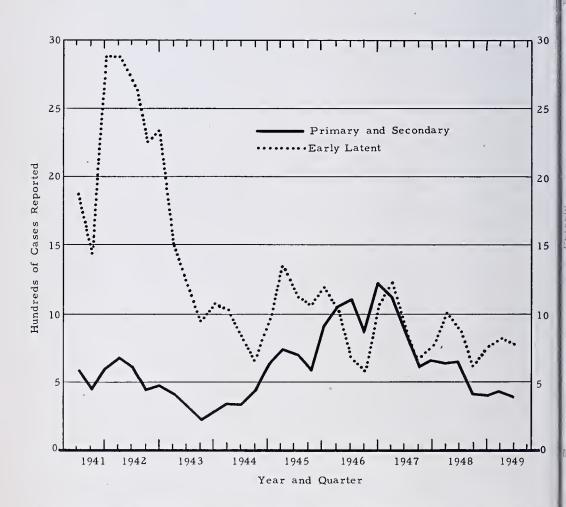


FIGURE. 1—Trend of primary and secondary and early latent syphilis reported by clinics and institutions in Mississippi, third quarter 1941 to third quarter 1949.

increasing paresis rate in some southern States in spite of decreases in other factors. In table 1 the trends of mental hospital admissions and mortality due to syphilis in Mississippi are indicated. For the United States as a whole, the trend is downward for insanity as well as mortality. for this purpose, we have used the reports of clinics and institutions. The trend for primary and secondary syphilis is downward from the first quarter of the calendar year 1947 for both white and nonwhite and is now approximately

⁵ Number of cases occurring during a period.

the same as in 1942. We believe that this indicates a decrease in the real incidence of syphilis as the number of cases of early latent syphilis reported has also decreased, and there has been no diminution in case-finding activities for early syphilis (fig. 1). This trend is in agreement with the national trend.

it is necessary to determine in advance what constitutes the existence of the disease. For syphilis, the number of persons with a positive result to the serologic test for syphilis is frequently considered as an estimate of the prevalence of syphilis. This is usually based on a rationalization that the number of positive

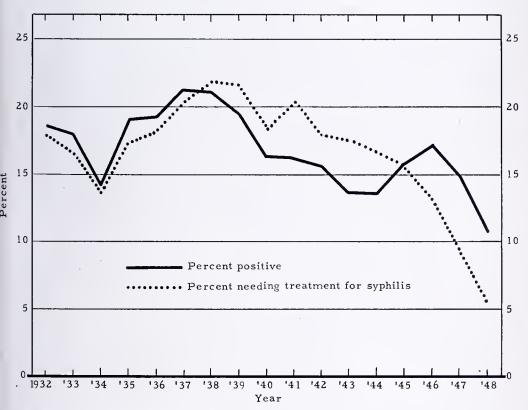


FIGURE 2.—Percent infected of nonwhite women examined for syphilis at first admission to prenatal clinics in Mississippi, 1932-48.

Prevalence

The prevalence of a disease is usually defined as the amount of the disease in existence at any particular time. It is variously referred to as "the extent of the problem," the "potential treatment load," and so on. In attempting to measure the amount of a disease in existence,

cases that do not have syphilis now will be balanced by the number with syphilis whose result to the test is negative. Moreover, after 14 years of intensive case finding there will exist in the community many persons whose blood test still shows a positive reaction but who have been adequately treated. It is believed, however, that the trend of the number of persons with a positive serologic test for syphilis is indicative of the direction of the trend of the prevalence of syphilis. A preferable definition, but a measure-

⁶ Bauer, T. J.: Is the Incidence of Syphilis Decreasing? Editorial. J. Ven. Dis. Inform., 30: 185-186, July 1949.

ment more difficult to obtain, is the number of persons with syphilis needing treatment.

It is important, in selecting a group the result of whose examination is known over a period of years, that selection be made on the basis of some factor not connected with syphilis, if any generalization is to be made. We decided that pregnant women being tested as part amination on the *first* admission to the prenatal clinic. To obtain the data we abstracted the records of five prenatal clinics in Mississippi, of which two have records back to 1932; one, to 1934; one, to 1938; and one, to 1942.

As another unit of measurement of trend we recorded for each woman the doctor's recommendation regarding the necessity for antisyphilitic therapy. In

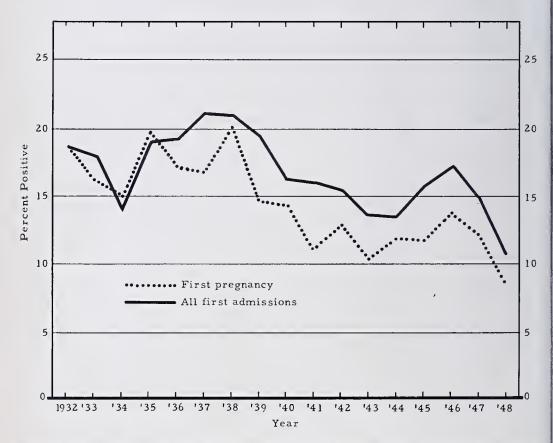


FIGURE 3.—Percent positive in first pregnancy, and percent positive of first admissions to prenatal clinics in Mississippi (nonwhite women examined for syphilis), 1932-48.

of their prenatal examination may be an unbiased group regarding presence of syphilis in pregnant women. Because case finding among pregnant women may be more effective than among the general population, trends in the prevalence of syphilis in women having their second or later babies may not be indicative of the trend in the population. We therefore will present the data on the result of ex-

some instances, where no written recommendations appeared on the patient's chart, administration of treatment was taken as signifying necessity for treatment. Recommendation of treatment for syphilis in pregnancy may differ from recommendation of treatment for syphilis in nonpregnant women, especially in the era of arsenicals. It is probable that in recent years many pregnant women with presumably adequate treatment for syphilis prior to pregnancy have gone untreated during pregnancy. This factor should be considered when examination is made of the trend of syphilis needing treatment in pregnant women.

The maternity records of five county clinics were abstracted, starting with the following years: 1932, Pike County; 1932, Sunflower County; 1934, Lee County; 1938, Coahoma County; and 1942, Grenada County. Because of the small number of white persons attending these clinics the data will be presented for nonwhite only. The result given is the result of the examination at the time of the first admission for pregnancy, regardless of the result of subsequent examinations.

In table 2 and figure 2 are presented the results of the blood test on first admission to these clinics and the status regarding necessity for treatment. It

Table 2.—Results of examination of pregnant nonwhite women in Mississippi—first admissions to prenatal clinics, 1932–48

	Blood	1 test	Exami	nation
Year	Number tested	Percent posi- tive	Number exam- ined	Percent needing treat- ment
1932	204	18.6	202	17.8
1933	487	17.9	479	16.5
1934	534	14.0	531	13.6
1935	506	19.0	496	17.3
1936	526	19.2	519	18.1
1937	645	21.2	637	20.3
1938	785	21.0	793	21.8
1939	1, 191	19.5	1, 220	21.5
1940	1, 035	16. 2	1, 059	18.4
1941	982	16.1	1,033	20. 4
1942	1, 055	15.6	1,082	17.
1943	933	13.6	974	17. 5 6
1944	853	13.5	890	16. 00
1945	789	15.8	803	15. 6
1946	1,148	17.3	1,152	13.3
1947	1,340	14.9	1,336	9.4
1948	1,000	10.9	994	5.6

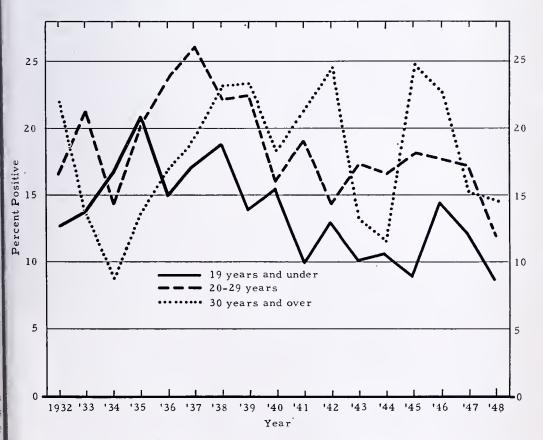


FIGURE 4.—Percent positive of first admissions to prenatal clinics in Mississippi (nonwhite women examined for syphilis), by age group, 1932-48.

will be noted that during the period 1938 through 1944, the number of women with syphilis needing treatment exceeded the number of women with positive results to the serologic test for syphilis, but that since 1946 the situation has reversed. Both sets of data show decreases since 1938, with positive bloods showing an increase during 1945 and 1946.

No significant difference is noted between the results of examination of the first pregnancy as contrasted to the first admission for pregnancy.7 From the data shown in figure 3, it will be noted that the trend is approximately the same as in figure 2. Presumably, therefore, the trend of prevalence of syphilis in young nonwhite women in Mississippi has been downward since 1946 and is only approximately half what it was in 1938. It may be noted that the rate is lower for women having their first baby than it is for those having subsequent babies. This may be accounted for by the fact that they are younger and the fact that in women having second and subsequent babies, the examination is on the first admission to prenatal clinics.

In considering the results of examination by age (fig. 4) it is noted that the trend is downward in the three age groups—19 years and under, 20 through 29 years, and 30 years and over. Presumably any downward trend in the prevalence of syphilis is not caused by variation in the age composition of women having babies. It is noted that the prevalence rate is lower in the "under 20" group, which agrees with the lower rate in women having their first baby.

Summary

- 1. The trend of recorded mortality from syphilis in Mississippi is downward.
- 2. The trend of recorded infant mortality from syphilis is downward.
- 3. The trend of admissions to mental institutions with psychoses due to syphilis shows no downward trend.
- 4. The trend of the reported incidence of syphilis has been downward for the past 3 years.
- 5. The trend of the prevalence of syphilis, as indicated by the trend in pregnant women receiving prenatal care in public clinics, has been downward since 1947; the figure for 1948 is the lowest recorded since 1932.

⁷ The result recorded for all persons is that of the initial examination for pregnancy in the clinic. Some of these first admissions were for the first pregnancy, some for the second, and so on.

The Ohio National Guard Blood-Testing Program

Charles R. Freeble, Jr., M. D., Earl O. Wright, James F. Donohue, and John B. Bolin

At the Regional Venereal Disease Seminar of the United States Public Health Service held in Washington, D. C., early in 1949, the possibility of blood testing all National Guardsmen during the 1949 summer encampment period was discussed as a case-finding technic and as a method of estimating syphilis prevalence.

After studying the summer encampment program of the Ohio National Guard it was decided that such a plan was not feasible in Ohio. Summer encampment locations were scattered throughout the State, and several units were to be stationed outside the State in Indiana and Such dispersement of the Delaware. troops within and outside the jurisdiction of the Ohio Department of Health, plus the fact that the summer encampment schedule was crowded into a busy 2-week schedule, made impossible a bloodtesting program at summer encampment. Another approach to the problem was therefore necessary.

A cooperative program was agreed upon between the Ohio Department of Health and the Adjutant General's Department of the Ohio National Guard. Blood samples of all men in a particular unit were to be drawn by personnel of the local health department during a regularly scheduled drill period of the unit. The program was scheduled to be accomplished during the period April 15 to July 1, 1949, prior to the time at which National Guardsmen in Ohio encamp for summer maneuvers. The success of such

a program depended, of course, on 100percent participation of every local health department and every unit of the Ohio National Guard. This plan went into motion during March 1949, when all commanding officers of the National Guard were directed by the adjutant general to contact the local health commissioner in their areas to make immediate arrangements for having the blood samples The adjutant general also didrawn. rected the commanding officer of each unit to furnish copies of his complete roster to the Ohio Department of Health to facilitate the program.

All local health commissioners were advised of the program by a series of memoranda from the director of health. These communications outlined the program, suggested procedures, furnished copies of the rosters of the members of all units in each health jurisdiction, and urged each health commissioner to cooperate with the program. It was suggested that each health commissioner establish a plan within his own department for obtaining the blood specimens.

Where required, blood tubes and mailing kits were provided by the Ohio Department of Health Laboratory. Health departments with laboratory facilities performed the tests, and health departments without the necessary personnel and equipment used the services of the Ohio Department of Health Laboratory in Columbus. It was agreed that any infected individual, regardless of the stage of disease, could be immediately admitted to the Central Ohio Rapid Treatment Center unless he preferred to secure treatment from a private physician.

By and large, this plan was satisfactory, and most of the health departments cooperated. However, one of the largest city health departments in Ohio did not have enough personnel to draw the blood specimens but agreed to run the tests.

¹ Chief, Division of Communicable Diseases, Ohio Department of Health.

² Division of Communicable Diseases, Ohio Department of Health.

³ Health Program Representative, U. S. Public Health Service.

⁴ Division of Communicable Diseases, Ohio Department of Health.

Blood kits were furnished to the medical units of the National Guard, and personnel attached to medical units drew blood specimens from several other units. This arrangement did not prove to be entirely satisfactory, however, and less than 50 percent of the guardsmen in this area were tested. Some health commissioners solved the problem of personnel by a cooperative program with the county medical society. Physicians donated their services and drew the blood specimens. This method, which succeeded in testing 100 percent of the guardsmen in one area, is a fine example of what can be done through cooperation between the health department and the county medical society.

In many of the part-time and unorganized health areas it was necessary for a blood-testing team from the Ohio Department of Health to go to the local armory and draw the bloods during drill period. The team consisted of a venereal disease investigator who served as coordinator and two senior medical students who drew the blood specimens. Clerical and nursing help was provided in these areas by either the health department or guardsmen. This team served to draw all blood specimens in units located in 14 Ohio cities.

Most of the National Guard units were very cooperative in making the men available for blood tests during drill hours. However, since most of the blood testing in any particular unit was done by the health department during one single drill period, it was not possible to test the full complement because of absenteeism due to sickness, employment, or evasion of the test. One large unit of about 400 men was not tested because of a change of officer personnel and a misunderstanding regarding the authority to draw blood specimens during an actual drill period when guardsmen were being paid for training.

Prior to this program, the induction physical examination of the new guardsmen did not include a blood test. However, serologic examination is now being considered for inclusion in the entrance

physical examination of all applicants to the Ohio National Guard, some units having already adopted this plan on a voluntary basis. The main problem in instituting this policy is apparently a shortage of medical officers. Thus it is noted that in certain areas, local health departments did not cooperate to the fullest extent possible and that in other areas, local guard units did not cooperate very well in the program. This lack of cooperation resulted in a considerable percentage of the National Guard members not being tested.

The Ohio National Guard is composed of 217 units, totaling about 12,000 members located in 84 cities in the State. The total number of persons tested was 7,508, which comprised 62.6 percent of the total members. The 61 positive serologic tests found among the total examined is equivalent to a syphilis rate (as detected by positive serology) of 8.1 per 1,000 persons tested.

Table 1 shows a break-down of the results of this blood-testing program by race and age where these factors are known. The syphilis rate among Negro guardsmen was significantly higher than that among the white troops. Table 2 presents the results of the tests by age group only. It will be noted in both tables that, in general, the syphilis prevalence rate increases as age increases. This observation might be expected since the number of syphilis cases in a population would be cumulative with age unless all cases were discovered and adequately treated in the primary or secondary stage.

It is interesting to compare the indices of syphilis prevalence in 1949 as determined by this serologic survey among Ohio National Guardsmen with those of syphilis prevalence as measured by serologic tests among selectees and volunteers in Ohio from November 1, 1940, through April 15, 1941. Both groups are made up of young men in Ohio with no data related to socioeconomic or educational background. The only known difference in the two groups is the fact that the guardsmen are all volunteers

Table 1.—Prevalence of syphilis detected by positive serologic blood tests among members of the Ohio National Guard, by race and age, 1949

Age (years)	Total number of per- sons tested	Total number of persons in whom syphilis was detected by positive serology	Syphilis rate (de- tected by positive serology) per 1,000 persons tested
•	WHIT	E	
18–20 21–25 26–30 31–35	2, 894 1, 424 763 429 209	9 5 8 3 4	3. 1 3. 5 10. 5 7. 0 19. 2
Total	5, 719	29	5. 1
Other or unknown age	1, 505	13	8.6
Total (all ages) _	7, 224	42	5.8
	NEGI	RO	
18-20 21-25 26-30 31-35 36-40	117 53 46 26 12	7 3 1 1 3 2	59. 8 56. 6 21. 7 115. 4 166. 7
Total	254	16	63.0
Other or unknown age	30	3	100.0
Total (all ages)	284	19	66. 9
Grand total	7, 508	61	8.1

Table 2.—Prevalence of syphilis detected by positive serologic blood tests among members of the Ohio National Guard (white and Negro), by age, 1949

Age (years)	Total number of per- sons tested	Total num- ber of per- sons in whom syphilis was de- tected by positive serology	Syphilis rate (de- tected by positive serology) per 1,000 persons tested
18-20 21-25 26-30 31-35 36-40	3, 011 1, 477 809 455 221	16 8 9 6 6	5. 3 5. 4 11. 1 13. 2 27. 1
Total	5, 973	45	7.5
Other or unknown age	1, 535	16	10. 4
Total (all ages)	7, 508	61	8.1

for duty and are men desiring to serve the military needs of the State and Nation, whereas the selectees were required to be examined in the draft in the early period of World War II.

A comparison of table 1 with table 3 shows a striking difference in syphilis rates per thousand persons tested. In both the white and Negro groups the 1949 syphilis rates, as determined in the National Guard program, were significantly

Table 3.—Prevalence of syphilis detected by positive serologic blood tests among selectees and volunteers in Ohio, by race and age, November 1, 1940, to August 31, 1941 ¹

Total

number

of per-

sons

bateat

Age (years)

Total num-

ber of persons in

whom

syphilis

was de-

Syphilis

rate (detected by

positive

serology)

	tested	tected by positive serology	per 1,000 persons tested
Total all races_	139, 712	3, 609	25. 8
	WHIT	E	
18-20	1, 152	5	4.3
21-25	68, 587	504	7.3
26-30	31, 665	594	18.8 38.9
31 - 35 36-40	16, 744 857	651 45	52. 5
00-10			02.0
Total	119,005	1, 799	15. 1
18-20	70	37	0
18-20	3,054 1,547 856	37 49 70 4	12. 3 31. 8 81.
21-25 26-30 31-35	3,054 1,547 856	49 70	31. 31. 81. 74.
21-25	3,054 1,547 856 54	160	0 12.1 31.7 81.8 74.1
21-25 26-30	3,054 1,547 856 54 5,581 NEGI	160	12.1 31.3 81.8 74.1
21-25 26-30	3,054 1,547 856 54 5,581 NEGI	49 70 4 160 RO	12.1 31 81.8 74.1 28.7
21-25 26-30	3,054 1,547 856 54 5,581 NEGI	188 377 458	12. 31. 81. 74. 28.
21-25 26-30	3,054 1,547 856 54 5,581 NEGI	160 RO	12. 31. 81.: 74. 28. 57. 105. 184. 262.
21-25 26-30	3,054 1,547 856 54 5,581 NEGI 312 3,561 2,480 1,931	188 377 458	12. 31. 81.: 74. 28. 57. 105. 184. 262.
21-25 26-30	3,054 1,547 856 54 5,581 NEG1 312 3,561 2,480 1,931 139	160 RO	12. 31. 81. 74. 28. 57. 105. 184. 262. 215.
21-25 26-30	3,054 1,547 856 54 5,581 NEG1 312 3,561 2,480 1,931 139	18 377 458 506 30	12. 31. 81. 74. 28.

¹ Results of Serological Blood Tests for Syphilis on Selective Service Registrants, Based on the First Million Reports Received November 1, 1940, to April 15, 1941. U. S. Public Health Service, table 1A, p. 310. Results of Serological Blood Tests for Syphilis on Selective Service Registrants, Based on the Second Million Reports Received April 16, 1941, to August 31, 1941. U. S. Public Health Service, table 1A, p. 310.

lower than the rates among selectees and volunteers in 1940 and 1941. The marked difference in rates in both color groups might be explained by the following three considerations: (1) The National Guard group possibly is composed of select men with higher ideals and morals than the selectees; (2) there has been, in fact, a decrease in syphilis among young men in Ohio between 1941 and 1949, which theory might be supported by the downward trend of syphilis morbidity reporting in Ohio; (3) the guardsmen who were not tested because of absenteeism may represent men who failed to volunteer for the blood test because they feared detection of syphilis. It is also possible that the difference in rates can be explained by a combination of the above factors.

In order to investigate whether absenteeism among guardsmen affected the results of the study, it is proposed to carry out a special blood-testing program in several units wherein absenteeism was noticed. All men who were not blood-tested previously would be required to submit to a blood test. A study of the results of these tests among absentees would therefore determine whether absenteeism caused a lower detection rate than would have been found with 100-percent participation. This special phase of the study would also serve to

indicate, in general, whether persons who fail to take a blood test in any volunteer mass blood-testing program are trying to evade detection of syphilis or do not cooperate for other reasons.

Summary of Results

- 1. A voluntary blood-testing program was done among Ohio National Guard members from April 15 to July 1, 1949. The total number of men tested was 7,508, which comprised 62.6 percent of the total roster.
- 2. Failure to secure a greater number of tests was caused by absenteeism and lack of cooperation on the part of some local health departments and some units of the National Guard.
- 3. There were 61 positive serologic tests, which represents a detection rate of 8.1 per 1,000 persons tested.
- 4. Syphilis detection rates in this program were significantly lower than those among selectees and volunteers during World War II.
- 5. A blood test is now being considered as part of the physical examination of all men enlisting in the Ohio National Guard.
- 6. Further study is proposed among guardsmen who were absent during the test to determine whether absenteeism was a factor in the low detection rates.

Treatment of Early Syphilis With Three Injections of Penicillin and With One Injection of Penicillin. II.¹

R. D. Wright, M. D.;² F. P. Nicholson, M. D.;³ and R. C. Arnold, M. D.⁴

While it has now been well established (1) that maximum cure rates may be expected in early syphilis if the regimen maintains therapeutic blood levels of penicillin for not less than 72 hours, a number of questions remain to be answered.

What is an effective blood level of penicillin? What are the lower and upper limits of penicillin concentration for best possible control of those several inconstant factors in the host, the organism, and the drug itself that apparently modify the action of penicillin in human syphilis? What are the practicable means for measuring the range of effective penicillin concentration and, consequently, for establishing the most generally effective dosage for single-injection therapy of early syphilis?

There have been many approaches in clinical and experimental research to determining the answers to these questions. The findings of the various studies leave us in little doubt that a single-injection schedule utilizing a slowly absorbed penicillin preparation can be established for effective and practical use in the therapy of early syphilis.

At the Venereal Disease Research Laboratory, extensive studies of blood serum levels have been made after the injection of various amounts and kinds of procaine penicillin. The findings parallel and con-

firm those of Kitchen (1) and others as to the remarkably sustained serum levels possible with microcrystalline procaine penicillin G in peanut oil containing 2 percent of aluminum monostearate.

In studies utilizing the experimental schedule of 200,000 units of aqueous penicillin every 2 hours for 36 injections, Arnold and Mahoney demonstrated that early syphilis can be cured if therapeutic penicillin blood levels are maintained for 72 hours (2). This excessive dosage was employed in order to eliminate the dosage factor while establishing the time factor.

Serologic and clinical results obtained when 451 patients were treated with this 36-injection schedule of aqueous penicillin are presented in table 1. As the table shows, the cumulative re-treatment rate is 6.3 percent and seronegativity rate is 84.3 percent by the thirty-sixth posttreatment month. However, if probable reinfections are excluded from the cases re-treated, the cumulative failure rate is only 1.1 percent from the fifth month of observation through the thirty-sixth month. As other investigators have observed, the incidence of reinfections continues to obscure the evaluation picture as therapy becomes faster and more simplified.

No cases were re-treated on the basis of serologic failure alone. If the 1.1 cumulative failure rate is accepted as an indication of the true therapeutic response obtainable with this schedule, it appears unlikely that a lower failure rate will be obtained with penicillin until knowledge of the drug's therapeutic action and of the biology of syphilis is broadened beyond the present scope.

Following the demonstration that early syphilis can be cured with 3 days of adequate penicillin concentration, studies were undertaken at the Venereal Disease

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⁴ Medical Director, Chief, Technical Services Branch, National Heart Institute, U. S. Public Health Service; formerly with the Venereal Disease Research Laboratory.

Table 1.—Serologic and clinical results of treating early syphilis with 200,000 units of aqueous crystalline penicillin G every 2 hours for 36 hours

				Patie	nts re	-treated				Patie	ents no	ot re-tre	ated	
Observation period	Clinical relapse Probable reinfection						Total 1			Seropo	sitive	Seronegative		Total patient ob-
(months)	Num- ber	Per- cent	Cumu- lative percent	Num- ber	Per- cent	Cumu- lative percent	Num- ber	Per- cent	Cumu- lative percent	Num- ber	Per- cent	Num- ber	Per- cent	served
0	2 1 1 1		0.5 .5 .8 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1	1 2 2 2 1 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1	0.3 .5 .6 .6 .3 .7 .3 .7 .3 .4 .4 .5	0.3 .8 .8 .8 1.4 2.0 2.3 3.0 3.3 3.3 3.3 3.3 3.3 3.3 3.7 4.1 4.6 4.6 4.6 4.6 5.2	3 2 1 1 2 2 1 2 1 2 1 1 1	-0.8 .5 .3 .3 .6 6 .3 .7 3 4 .5	0.8 1.3 1.6 1.9 2.5 3.1 4.1 4.1 4.4 4.4 4.4 4.4 4.8 5.2 5.7 5.7 6.3	342 303 258 228 198 167 141 118 103 90 76 647 39 32 31 27 24 20 18	88. 6 79. 1 69. 9 64. 5 57. 0 44. 5 43. 1 37. 0 32. 6 25. 5 22. 2 317. 8 15. 3 11. 3 11. 7 10. 3 9. 7	44 77 106 120 143 162 178 191 200 202 210 211 207 206 205 202 193 188 177 169 163 157	11. 4 20. 1 28. 7 33. 9 41. 1 48. 0 54. 4 59. 9 63. 7 66. 3 70. 4 73. 3 77. 8 80. 3 82. 5 82. 0 82. 8 83. 9 84. 9	38 38 36 35 34 33 32 31 31 30 29 28 27 26 25 24 21 20 19 18 17
4 5-27 8-30 1-33 4-36			1. 1 1. 1 1. 1 1. 1 1. 1			5. 2 5. 2 5. 2 5. 2 5. 2 5. 2			6.3 6.3 6.3 6.3 6.3	14 13 8 7 2	8. 9 9. 3 8. 1 13. 1 9. 4	133 118 85 43 18	84. 7 84. 4 85. 6 80. 5 84. 3	18 14 9 8

¹ None were re-treated on the basis of serologic failure.

Research Laboratory to determine the results of administering varying amounts of procaine penicillin G in peanut oil containing 2 percent of aluminum monostearate. Observations of the average penicillin levels obtained and of patients recently treated with one-injection and three-injection schedules were subsequently presented (3). Posttreatment observation for more than a year on the results of two of the schedules are now offered with certain conclusions.

Patients with primary or secondary syphilis were carefully selected according to the following criteria: All patients were darkfield positive (those diagnosed as secondary were darkfield positive from secondary lesions); no patient had a history of previous syphilis; and no patient had received antisyphilitic or penicillin therapy for any condition within the 3 months preceding his antisyphilitic therapy.

Figure 1 shows the average penicillin blood levels obtained in a group of 112 patients (not necessarily syphilitic patients) treated once daily for 3 days with 600,000 units of procaine penicillin G in peanut oil containing 2 percent of aluminum monostearate. At 72 hours, 100 percent of the patients showed a penicillin blood level of 0.015 or more units per cubic centimeter of serum. The average level was 0.306. Ninety-six hours after the initial injection, 11 percent of the group failed to show a detectable level, but among the remaining 89 percent the average was 0.166 units of penicillin per cubic centimeter of serum.

The therapeutic results obtained when 97 patients who met the study criteria were treated with this 3-day penicillin schedule are presented in table 2. The cumulative re-treatment rate is 11.5 percent, which includes a probable reinfection rate of 8.6 percent. As indicated,

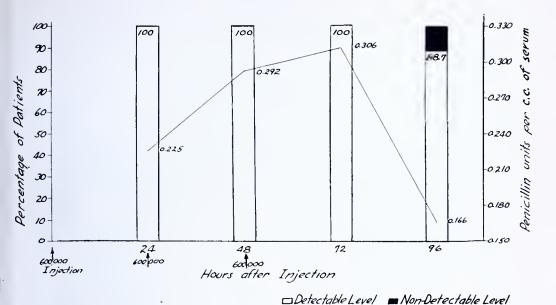


FIGURE 1.—Average blood levels of 112 patents (not necessarily syphilitic patients) treated once daily for 3 days with 600,000 units of procaine penicillin and aluminum monostearate.

Table 2.—Serologic and clinical results of treating early syphilis with 1 injection daily for 3 days of 600,000 units of procaine penicillin and aluminum monostearate

				Patie	nts re	-treated				Patie	ents n	ot re-tre	ated	
Observation period	Serc	ologic	failure	Pro	bable fectio			Tota] 1	Sero ti	posi- ve	Seron		Total patients
(months)	Num- ber	Per- cent	Cumu- lative per- cent	Num- ber	Per- cent	Cumu- lative per- cent	Num- ber	Per- cent	Cumu- lative per- cent	Num- ber	Per- cent	Num- ber	Per- cent	ob- scrved
1	1 1		1. 4 2. 8 2. 8 2. 8 2. 8 2. 8 2. 8 2. 8 2. 8	1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1. 4 2. 8 1. 4 1. 4	1. 4 4. 2 5. 6 7. 0 7. 0 8. 6 8. 6 8. 6 8. 6 8. 6 8. 6 8. 6 8. 6	1 3 2 1	1. 4 4. 2 2. 9 1. 4	1. 4 5. 6 8. 5 9. 9 9. 9 11. 5 11. 5 11. 5 11. 5 11. 5 11. 5 11. 5 11. 5	72 63 59 46 39 28 27 24 21 15 13 13 11 11 10 8 7 4 4 1	86. 7 76. 8 62. 2 54. 9 39. 4 38. 6 34. 3 31. 0 22. 9 20. 5 22. 1 19. 1 20. 3 19. 7 16. 9 16. 3 12. 2 8. 8	11 19 19 28 31 39 37 39 40 44 43 39 40 37 35 31 25 31 9 31 32 31 31 32 31 31 32 31 31 31 31 31 31 31 31 31 31 31 31 31	13. 3 23. 2 24. 4 37. 8 43. 7 54. 9 55. 8 59. 1 67. 2 68. 0 66. 4 69. 4 68. 8 71. 6 72. 2 76. 3 79. 6 88. 5	83 82 78 74 71 71 70 70 68 66 63 59 58 54 51 47 43 33 19

¹ No cases were considered to be clinical relapses.

no cases were considered to be clinical relapses. Two patients were re-treated for serologic failure, with a cumulative re-treatment rate of 2.8 percent.

Although the group of patients in whom this schedule was observed is small, the schedule appears to be a practical and satisfactory 3-day ambulatory regimen, as might be expected from the high average penicillin blood levels obtained and shown in figure 1.

Another schedule was studied consisting of one injection of 300,000 units of the procaine penicillin and aluminum monostearate. This regimen was investigated in an effort to discover the minimum amount of slowly absorbed penicillin that would prove adequate in a single-injection schedule.

As shown in figure 2, at 72 hours a detectable concentration of penicillin was observed in the serum of 97 percent of 374 patients (not necessarily syphilitic patients), their average blood level being 0.042 unit of penicillin per cubic centimeter of serum.

Table 3 reveals the results obtained when 123 patients who met the study criteria were treated with this one-injection schedule. These results are not satisfactory. At the thirteenth month, the cumulative re-treatment rate is 19 percent, which includes a higher rate of serologic failures (11.5 percent) and of clinical relapses (5.2 percent) than of probable reinfections (2.3 percent).

Figure 3 shows the cumulative retreatment rates of the patients meeting the study criteria who were treated with the three schedules discussed in this pa-The total cumulative re-treatment rates are shown for each schedule by months, as well as the re-treatment rates minus probable reinfection rates. eighth posttreatment month, more than 50 patients remained under observation in each schedule, and the majority of re-treatments had been administered. Excluding probable reinfections from the total number of cases re-treated, a significant difference is observed at the 5-percent level between the two schedules using procaine penicillin G in aluminum monostearate; that is, at 8 months, the three-injection schedule was significantly better in terms of true therapeutic response than the one-injection schedule using only 300,000 units.

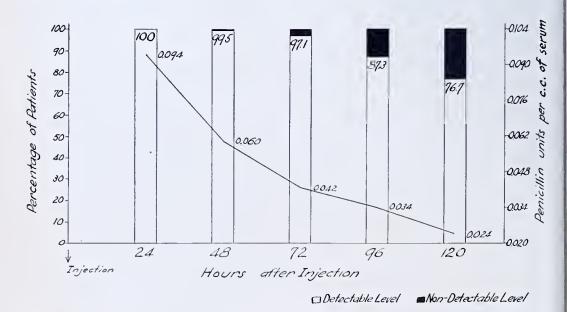


FIGURE 2.—Average blood levels of 374 patients (not necessarily syphilitic patients) treated with one injection of 300,000 units of procaine penicillin and aluminum monostearate.

Table 3.—Serologic and clinical results of treating early syphilis with 1 injection of 300,000 units of procaine penicillin and aluminum monostearate

					Pati	ents	re-treat	ted					Patie:	nts no	ot re-tre	eated	
Observa-		rologi ilure	e		linical lapse			obabl ifectio		7	Γotal		Sero		Seron		Total
tion period (months)	Num- ber	Per- cent		Num- ber	Per- cent		Num- ber	Per- cent		Num- ber	Per- cent		ber	Per- cent	Num- ber	Per- cent	tients ob- served
1	3 1 1 1 1	1.2 1.4	4. 6 6. 0 7. 8 7. 8 7. 8 7. 8 7. 8	2 2		5. 2 5. 2 5. 2 5. 2 5. 2 5. 2 5. 2 5. 2			1.1 2.3 2.3 2.3 2.3 2.3 2.3 2.3 2.3 2.3 2.3	3	1.8	4. 5	18 12 9 6 6 6 4 3 2	70. 7 59. 8 50. 6 42. 3 36. 3 26. 9 21. 2 19. 1 15. 4 18. 8 14. 7 17. 4 16. 2	29 36 40 40 36 40 36 31 27 25 21 18 11 8	29. 3 39. 1 45. 0 48. 4 50. 2 59. 7 63. 6 65. 7 69. 3 68. 3 65. 9 66. 3 63. 7 64. 9	99 92 89 83 72 67 57 47 39 37 32 27 17 12

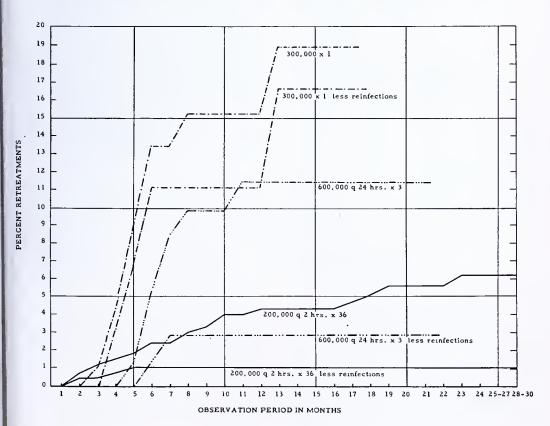


FIGURE 3.—Cumulative re-treatment rates among patients who met the study criteria and who were treated with three penicillin schedules.

Conclusions

On the basis of these studies:

- 1. A single injection of 300,000 units of procaine penicillin G in peanut oil containing 2 percent of aluminum monostearate does not provide an optimum cure rate in early syphilis (123 cases, 51 percent follow-up at the end of 6 months).
- 2. The schedule of 600,000 units daily for 3 days offers an effective and adaptable regimen for the ambulatory treatment of early syphilis (97 cases, 70 percent follow-up at the end of 6 months).

References

- KITCHEN, D. K.; THOMAS, E. W.; REIN, C. R.: Serum concentrations following five treatment schedules with procaine penicillin in oil with aluminum monostearate. J. Invest. Dermat., 12: 111– 115, February 1949.
- Arnold, R. C.; Mahoney, J. F.; Nicholson, F. P.; Wright, R. D.: Penicillin therapy of early syphilis: IV. J. Ven. Dis. Inform., 30: 125-127, May 1949.
- 3. WRIGHT, R. D.; NICHOLSON, F. P.; MA-HONEY, J. F.; ARNOLD, R. C.: The treatment of early syphilis with three injections of penicillin and with one injection of penicillin. A Symposium on Current Progress in the Study of Venereal Diseases. Washington, D. C., April 1949. Pp. 28-34.

CURRENT NOTES AND REPORTS

WHO Publishes Three VD Reports

The World Health Organization of the United Nations has published the report of its Expert Committee on Venereal Infections, which held its third session in Washington, D. C., October 10–20, 1949. The nine Committee members—Dr. W. E. Coutts (Chile), Dr. R. Degos (France), Dr. M. Grzybowski (Poland), Dr S. Hellerstrom (Sweden), Dr. E. H. Hermans (Netherlands), Dr. G. L. M. McElligott (United Kingdom), Dr. J. F. Mahoney (U. S. A.), Dr. I. H. Nagi (Egypt), and Dr. R. V. Rajam (India)—made six major recommendations to the World Health Organization.

The Expert Committee recommends:

- 1. That WHO proceed cautiously toward the long-term objectives, and that priority be given to economically underdeveloped areas with a high prevalence of syphilis and/or other treponematoses.
- 2. That the 1950 program form the basis for activities in 1951 and 1952, so as to enable consolidation of the gains

obtained; development of polyvalent services in Nation-wide programs and in demonstration areas following initial venereal disease operational activities is desirable, with particular emphasis on maternal and child health, and health education.

- 3. That emphasis be placed on assisting countries to establish in their health administrations at least a basic venereal disease control structure headed by a health officer specializing in venereal disease control.
- 4. That WHO support selected venereal disease training activities in regions where limited facilities are available, and the setting-up of regular training courses in training institutions under an organized fellowship program, preferably where such a program can become part of an over-all public educational system.
- 5. That WHO encourage the establishment of venereal disease literature units in health administrations and other suit-

able institutions; and continue to prepare and distribute to such units, under the WHO literature program, venereal disease literature, technical releases, and reference lists on clinical, epidemiologic, and other aspects of venereal disease control.

6. That the Director General appoint further corresponding members in different countries, and that these members make available to WHO and Committee members information on major technical developments in their respective countries.

The Subcommittee on Serology and Laboratory Aspects of the Expert Committee on Venereal Infections held its first session during the meeting of the Expert Committee. Members of the Subcommittee are: Mr. Ad Harris (U. S. A.), Dr. P. Krag (Denmark), Dr. R. Laporte (France), and Dr. I. N. Orpwood Price (United Kingdom). They recommend:

- 1. That WHO draw the attention of health administrations to the necessity of maintaining a national reference laboratory for serodiagnosis of syphilis to control and guide serodiagnostic performances of local laboratories.
- 2. That a study of preserved serums be initiated as soon as possible on the basis of a preliminary exchange system between the serology laboratories of the United States Public Health Service Venereal Disease Research Laboratory, Atlanta; the Institut Pasteur, Paris; the State Serum Institute, Copenhagen; and the Venereal Diseases Reference Laboratory, London.
- 3. That a plan be drawn up by subcommittee members, based on the above experience, for a world-wide system for standardization of seroreactions and antigens in syphilis, aiming at the establishment of one or a few centers, to be designated later, delivering control serums and standard antigens to regional and national serodiagnostic laboratory centers.
- 4. That a study be made by WHO of location and activities of the main lab-

oratory centers in various countries where serology in syphilis is carried out, including reactions employed.

The WHO Expert Committee on Venereal Infections recommended at its sccond session, in October 1948, that a temporary study group should be established. They recommended that a limited number of venereologists from Europe and other regions should be appointed: (1) to evaluate the venereal disease control methods in use in the United States and their importance in national and international programs; and (2) to study control methods currently in use in the United States with particular reference to penicillin treatment in syphilis.

The group of seven—Dr. J. M. Funes (Guatemala), Dr. E. I. Grin (Yugoslavia), Dr. P. C. Joulia (France), Dr. N. Jungalwalla (India), Dr. S. M. Laird (United Kingdom), Dr. P. V. Marcussen (Denmark), and Dr. T. Putkonen (Finland)—began their 6 weeks' tour of the United States on August 15, 1949.

Their report includes the history of the venereal disease control program in the United States, an evaluation of penicillin therapy, and research and education in venereal disease. Diagnostic and treatment facilities are discussed, as well as case-finding and case-holding technics.

The three publications may be purchased from the Sales Section, Palais des Nations, Geneva, Switzerland, or from local United Nations agents. United States, the agent is Columbia University Press, International Documents Service, 2960 Broadway, New York 27, The reports are a part of the World Health Organization Technical Report Series: No. 13, Expert Committee on Venereal Infections, Report on the Third Session (28 pp., \$0.20 each); No. 14, Expert Committee on Venereal Infections, Report on the First Session of the Subcommittee on Serology and Laboratory Aspects (39 pp., \$0.25 each); No. 15, Venereal-Disease Control in the USA, Report of the WHO Syphilis Study Commission (69 pp. \$0.45 each).

American Social Hygiene Association Chief Dies

With the sudden death of Dr. William Freeman Snow on June 12, 1950, a pioneer in the fight against venereal disease has fallen. His work over the past half century has contributed notably to the changing public attitude toward health and disease.

Dr. Snow was chairman of the Board of Directors of the American Social Hygiene Association, which he founded in 1914. He was also president of the International Union Against the Venereal Diseases.

After receiving his doctorate in medicine from Stanford University in 1900, Dr. Snow made postgraduate studies at Johns Hopkins and other universities here and abroad. He later returned to Stanford as university physician and professor of hygiene and public health.

In 1917, he was appointed by President Wilson as a member of the Council of National Defense and served also as Chairman of the Executive Committee of the United States Interdepartmental Social Hygiene Board. He was in charge of the Army's venereal disease prevention measures from 1917 to 1919, retiring with the rank of colonel. During World War II he was a member of the Interdepartmental Committee on Venereal Disease comprising representatives of the Army, Navy, Public Health Service, and other Federal agencies.

Dr. Snow was the California State Health Officer from 1908 to 1914, and president of the State and Provincial Health Authorities of North America during 1912 and 1913. Between 1924 and 1928 he served as chairman of the League of Nations Committee to Study Traffic in Women and Children. Later he became president of the National Health Council.



William Freeman Snow, M. D., 1874-1950

Dr. Snow lectured on preventive medicine at Johns Hopkins, New York, and Columbia Universities. For many years, he served as a consultant to the United States Public Health Service.

Dr. Snow was a member of the American Public Health Association, the American Medical Association, the National Education Association, the New York Academy of Medicine, and the American Association for the Advancement of Science.

Thousands of leaders in all parts of the world have gained a broader vision through Dr. Snow's work. He built his own memorial—a world-wide influence for clean and constructive individual, family, and community living.

CURRENT LITERATURE

AM. J. CLIN. PATH., BALTIMORE

Cardiolipin antigens in the serodiagnosis of syphilis. A comparison with standard tissue-extract antigens. Joe M. Blumberg, James B. Hartney, and Mary O. Dimmock. Am. J. Clin. Path., 20: 367-370, Apr. 1950.

Cardiolipin and tissue-extract antigens were compared as to degree of reactivity when tested against 2,010 syphilitic serums and 882 negative controls. Serums selected for examination came from the Neurosyphilis Treatment Center, Oliver General Hospital. Cardiolipin complement-fixation procedure gave the most favorable results. Cardiolipin antigens were highly reproducible, standardizable by chemical methods, and retained their activity through an entire working day.

AM. J. PUB. HEALTH, NEW YORK

Multiphasic screening examinations—an extension of the mass screening technique. Lester Breslow. Am. J. Pub. Health, 40: 274–278, Mar. 1950.

.A general description of multiphasic screening is given along with the problems of technical development such as mass application of some tests. The procedure, through which 20 to 30 cases of significant disease may be discovered in 1,000 persons, constitutes a practical approach to the present-day problems in preventive medicine.

Multiphasic screening. Editorials. Am. J. Pub. Health, 40: 324-325, Mar. 1950.

Examinations which might profitably be included should be determined by the fact that a technician can administer the test with only general supervision and interpretation of the results by a physician. A special advantage is that the health department which undertakes such a program is brought face to face with the problem of chronic disease and of acute illnesses of constitutional origin.

AM. J. SYPH., GONOR. & VEN. DIS., ST.

Untreated syphilis in the male Negro. Observation of abnormalities over sixteen years. Pasquale J. Pesare, Theodore J. Bauer, and Geraldine A. Gleeson. Am. J. Syph., Gonor. & Ven. Dis., 34: 201-213, May 1950.

Analysis of data on 231 untreated Negroes in Macon County, Ala., shows a higher mortality rate in each 10-year age group than among the 192 nonsyphilitic controls. Among those between ages of 25 to 54 years at time of first examination, more symptomatic and potentially disabling conditions were observed among the untreated in each of the three examinations. No noticeable differences in amount of disability could be demonstrated between the two groups in persons 55 years of age and over when first examined. This is the fourth report in this series.

Observations on the growth of the non-pathogenic Kazan strain of *Treponema pallidum* in embryonated hens' eggs of various ages. Merle Haanes, Richter H. Wiggall, and Edward D. DeLamater. Am. J. Syph., Gonor. & Ven. Dis., 34: 214-218, May 1950.

Inoculation of 333 eggs divided among six age groups showed embryos 2 days old did not support well the growth of the Kazan strain. Use of 10- and 15-day-old embryos appeared to give the best results. No noticeable difference was shown between the yolk or albumin as a site for inoculation.

The effect of subcurative penicillin therapy upon the rate of development of acquired immunity in experimental syphilis. Harold J. Magnuson, Frederick A. Thompson, Jr., and Barbara J. Rosenau. Am. J. Syph., Gonor. & Ven. Dis., 34: 219-226, May 1950.

Purpose of this study, done at Syphilis Experimental Laboratory, University of North Carolina, was to test in experiAm. J. Syph., Gonor. & Ven. Dis., St. Louis—Continued

mental animals the validity of the hypothesis that a treated but uncured incould produce demonstrable degrees of immunity, and to measure the rate of development of such immunity in comparison with that produced by the unaltered infection. Results showed that in rabbits during the subcurative infection additional acquired immunity may develop at an estimated rate of one-sixth that of untreated infection. Data suggest that older treatment methods may have permitted development of more immunity than intensive treatment.

Pathologic observation of penicillin-treated neurosyphilis. George D. Gammon, F. H. Lewey, H. Dillon, Gabriel Schwarz, and John H. Stokes. Am. J. Syph., Gonor. & Ven. Dis., 34: 227–235, May 1950.

Of seven neurosyphilis patients autopsied at the University of Pennsylvania Hospital, one paretic who died 3 weeks after treatment showed the usual histology, while the others including paretics, meningovascular neurosyphilities and tabetics showed little inflammatory reaction. Evidence suggested that penicillin cleared the infection.

Pulmonary arteritis due to acquired syphilis. Milton R. Hejtmancik, James Y. Bradfield, and R. H. Rigdon. Am. J. Syph., Gonor. & Ven. Dis., 34: 236–244, May 1950.

Clinical and pathologic study is reported of a 56-year-old Negro woman with productive cicatricial pulmonary arteritis believed due to acquired syphilis. There was syphilitic aortitis involving the branches leaving the arch, which showed progression in spite of penicillin therapy.

Cardiolipin antigen in the Kline test for syphilis. III. Further studies on optimal cardiolipin-lecithin ratio. Sidncy J. Klein, B. E. Konwaler, Cecilia Sears, Meyer Berke, and George M. Leiby. Am. J. Syph., Gonor & Ven Dis, 34: 245– 261, May 1950.

Parallel battery tests were performed with antigens of varying ratios on 564 syphilitic and 621 nonsyphilitic serums with sensitivity varying directly and specificity inversely as the lecithin-cardiolipin ratio within the range tested. In tests on 658 known syphilitic serums, the Kline test with lecithin-cardiolipin ratio 8:1 proved much more sensitive than did standard Kahn and Kolmer tests. In tests on 13,304 presumably non-syphilitic serums, the cardiolipin (8:1) slide test showed a high degree of specificity and approached the excellent general specificity results obtained with the Kahn test.

Primary cutaneous Neisseria gonorrhoeae infections. Michael J. Scott and Joachim Thomsen. Am. J. Syph., Gonor. & Ven. Dis., 34: 262-264, May 1950.

Three case histories of gonococcic cutaneous penile infections are presented. It is believed more cases would be disclosed if routine smears and cultures were performed in all cases of cutaneous abscesses.

Antibiotic spectrum of the gonococcus. Thomas M. Gocke, Clare Wilcox, and Maxwell Finland. Am. J. Syph., Gonor. & Ven. Dis., 34: 265-272, May 1950.

Tests for sensitivity of 20 isolated strains of *Neisseria gonorrhoeae* were carried out with eight antibiotics and sulfadiazine. With few exceptions, the sensitivity of different strains for any one agent varied only moderately. Sensitivity of individual organisms to different agents varied quite markedly and independently. Antibiotics used were penicillin, aureomycin, Chloromycetin, streptomycin, bacitracin, neomycin, aerosporin, and polymyxin. Since this paper was submitted, 28 additional strains were tested with neomycin and terramycin.

Newer antibiotics in the treatment of venercal diseases. R. C. V. Robinson. Am. J. Syph., Gonor. & Ven. Dis., 34: 273-288, May 1950.

The in vitro activities of aureomycin and Chloromycetin on the causative agents and effects on experimental infection in laboratory animals are discussed. A comparative study of the effects in human infections of these drugs with other known effective therapeutic agents is made. Studies were made at Johns Hopkins Hospital.

BRIT. M. J., LONDON

A comparison of the Wassermann and Kahn reactions. T. E. Osmond. Brit. M. J., No. 4652: 524, Mar. 4, 1950.

Two series of Wassermann and Kahn tests were carried out on 2,223 and 2,298 serums. There was close agreement between the reactions and both showed a high degree of specificity. The finding of 2.2 percent positive reactions in pregnant women and 3.5 percent in diabetics indicated the advisability of routine tests on these persons.

J. INVEST. DERMAT., BALTIMORE

Serum concentration following the oral administration of crystalline procaine penicillin G. D. K. Kitchen, E. W. Thomas, and C. R. Rein. J. Invest. Dermat., 14: 229–231, Apr. 1950.

Data presented on the serum penicillin concentration produced by oral administration of tablets of crystalline procaine penicillin G differ widely from those obtained originally under the same conditions, but with the exception that a tablet of much higher compression was used in the original study. Numerical data on average serum concentrations for 23 patients are presented in tabular form.

Repository penicillin therapy of yaws in the Haitian peasant. A clinical and serologic survey. Charles R. Rein, Delmas K. Kitchen, and Edouard A. Pétrus. J. Invest. Dermat., 14: 239-246, Apr. 1950.

This study deals with results of treatment with a repository penicillin product of 1,200 Haitian peasants with early yaws. The clinical results obtained were consistently and invariably good. Although the majority of patients (92.1 percent) showed satisfactory serologic progress, only 316 had attained seronegativity at the end of a 12-month follow-up period.

M. Press, London

Some aspects of interstitial keratitis. T. L. de Courcy. M. Press, No. 4782: 198-201, Mar. 1, 1950.

The symptoms and cause of the disease are discussed. The author suggests local

treatment of atropine sulfate in 1-percent solution instilled twice daily in the eyes along with the antisyphilitic treatment. With better control of acquired syphilis, the disease should gradually disappear.

Mod. Hosp., Chicago

Personnel health service is good business. Some of the problems that must be considered when the hospital sets up its personnel health service. Sigmund L. Friedman. Mod. Hosp., 74: 63-64, 134, 136, 138, Apr. 1950.

Personnel health service is discussed as to the health clinic, preemployment examination, routine reexaminations, and special problems including venereal disease. There is no reason for discriminating against persons having a positive serologic test for syphilis. Whenever the disease is infectious, employment should be delayed or interrupted until a noninfectious state is reached through treatment

NORTH CAROLINA M. J., WINSTON-SALEM

Committee on venereal disease. A new dawn in venereal disease control. H. H. Henry. Committees and Organizations. North Carolina M. J., 11: 151-153, Mar. 1950.

Venereal disease education, contact investigation, legal aids, and the physician's responsibility in the venereal disease control program are discussed.

Pub. Health Nursing, New York

Prevention of congenital syphilis. Theodore J. Bauer and Hazel Shortal. Pub. Health Nursing, 42: 81–83, Feb. 1950.

A survey of the status of congenital syphilis and problems confronted in preventing it are presented. Duties of the public health nurses in helping to control the problem are discussed.

UROL. & CUTAN. REV., WEST PALM BEACH

The phenomenon of priapism: its diagnostic significance. A critical review. Fritz T. Callomon. Urol. & Cutan. Rev., 54: 144-150, Mar. 1950.

In certain rare cases of "syphilitic" priapism the syphilitic infiltration usually caused a state of permanent semierection.

STATISTICS

246

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, July to September 1949

[Known military cases excluded]

	<i>-</i>	o prior rter	Private physi- cian sources	1, 10 1, 28 1, 28 (*) 1, 05 1, 49	(*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	. 85 1. 27 1. 17 1. 17 1. 22 1. 22 1. 96	1.02 .93 1.14 .89	1.14 1.15 1.20 1.20 1.12
,	Gonorrhea	Ratio to prior quarter	All	1.13 1.30 1.09 (*) (*) 1.11 1.49			1.13 1.15 1.22 1.04	1, 17 1, 15 1, 12 1, 32 1, 10 1, 03
			rotal all sources	1, 151 280 71 645 15 79 61	11, 196 63 1, 323 6, 387 5, 417 a 3, 423 2, 505 302	15,952 4,871 1,994 4,450 3,013 1,240	7, 197 1, 671 2, 750 2, 776	8, 438 7, 074 5, 438 928 263 173
	d	Ratio to prior quarter	Private physi- cian sources	1.03 (*) (*) - 74 1.21		****1*1	(*) 1.02	€111€1
	Not stated	Ratio 1 qua	All	1.06	2. 13 (*) 62 (*). (*). (*).	%****1**1	1.07	€ €
	4	E	sources	116 36 1 0 0 32 47	351 30 455 53 444 0	95 10 10 10 10 10 10 10 10 10 10 10 10 10	240 12 228 0	000000
	l.	Ratio to prior quarter	Private physician sources	\$ £ £ £ £ £ £	8.8888	. I * I * * * * * * * * * * * * * * * *	(*) (*) 74 .98	.83 (*) (*) (*) (*) (*)
	Congenital	Ratio t	All	E.	(*) 1.05 1.05 1.05 65 65 84 (*)	(*) (69 (717 88 88 88 1818	1.05 .98 99 1.09	. 93 1. 24 1. 24 (*) (*)
	0	Total	all	23 20 12 12	312 66 156 106 37 84	260 177 177 22 23 93 38 70	358 49 93 216	234 116 67 74 12
	atent	o prior rter	Private physi- cian sources	0.84 1.09 (*) (*) (*) 1.03 1.03	**************************************	(*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	.82 .82 .82 .82 .82	. 78 . 84 . 83 . 90 . 58
Syphilis	Late and late latent	Ratio to prior quarter	All	0.83 1.01 .95 .70 (*) 1.10		. 75 86 65 77 77	92 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	88. .93. .93. .93. .93.
	Late	Total	sources	544 87 36 255 13 134 19	2, 662 938 3, 898 2, 960 2, 786 684 98	2, 089 343 621 621 454 269 370 486	3, 530 389 1, 072 2, 069	2,715 1,656 1,656 910 536 208 315
	nt	Ratio to prior quarter	Private physi- cian sources	9.82		. 62 (*) 44 . 31 . 55 . 55 . 53	. 89 . 87 1. 01 . 86	26.65 27.75 17.88 17.88
	Early latent	Ratio t	All	0.80 1.02 (*) (*) (*) (*)	.89 11.14 .83 .881 .881 .881 .75		92 98 88	. 88 . 98 . 73 . 73
	图	Tofal	all	180 58 119 67 6 6 6 28 28	2,767 73 714 1,057 966 923 740	2,060 242 363 363 231 717 475	1, 927 267 436 1, 224	1,362 964 723 277 37 84
	oudary	Ratio to prior quarter	Private physi- cian sources		(*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	(*) (*) (*) (*) (*) 1. 15 1. 15 . 66	.82 .59 .93	. 83 . 68 . (*) . (*)
	Primary and secondary	Ratio t	Ail	(*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	.96 (*) .97 .94 .93 .93	.91 .73 .82 .75 .75 .95	. 88 . 88 . 88	. 95 . 95 . 83 . 83 . 83 . 83 . 83
	Primar	Total	all	196 35 52 73 10 12	1,194 47 173 655 541 319 188 33	1, 411 121 287 165 165 478 299 299	836 208 277 351	854 617 338 183 13 41
		Federal Security Agency regions		Region 1—Total Connecticut. Maine. Massachusetts. New Hampshire. Rhode Island.	Region 2—Total Delawarc. New Jersey New York New York Pennsylvania. Philadelphia Philadelphia Philadelphia	Region 3—Total District of Columbia Maryland North Carolina Virginia West Virginia	Region 4—Total Kentucky——— Michigan————————————————————————————————————	Region 5—Total Illinois Chicago Indiana Minnesota Wisconsin

The Journal of Venereal Disease Information, September 1950

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Alabama—Alabam	Total continental	Total United States, including Territories

• Estimated. • From VM-820 except Philadelpbia July-September. • Ratio not calculated when base is less than 30. — Ratio not calculable. Base is zero or unknown.

by State and Territorial Health Departments, Cases of Syphilis and Conorrhea Reported to the Public Health Service October to December 1949

[Known military cases excluded]

æ		Ratio to prior quarter	Private physi- cian sources	0.73 73 74 38	(*) 84	933	. 29 89 1. 00 . 77 86		.85 1.27 .92 .93
Gonorrhea		Ratio t qua	All	0.78 .82 .90 .75 .92	.85 .85 .75	. 85 . 85 . 88 . 89 . 71	87.88.88.88.88.88.85.	. 76 . 76 . 87 . 95	. 25 28 88 88 88
		Total	sources	895 230 64 484 21 23	9,476	5, 410 4, 631 2, 222 2, 222 215	12, 935 3, 780 2, 002 1, 661 2, 517 901	6, 289 1, 271 2, 385 2, 633	6,488 5,323 4,154 763 249 153
	d	Ratio to prior quarter	Private physi- cian sources	(*) (*) (*) (*) (*)	(*)	XX	£1££1£1	(*) - 71	£111££
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	4	Total	0)	115 41 0 0 1 39 34	34	63 51 127 0	76 44 37 0 0	156 142 0	00000
	n]	Ratio to prior quarter	Private physi- cian sources	6.555555	1.03	1:11	. i * 1 * *	(*) (97 .73	. 86 1.14 (*) . 85 (*) (*)
	Congenital	Ratio t qua	All	# # # # # # # # # # # # # # # # # # #	1.11	1.31 1.46 1.07 1.08 (*)	1. 00 (*) (*) (*) (*) (*) 1. 11 1. 21 1. 21 1. 21	. 72 . 57 . 96 . 64	. 76 . 89 . 87 . 65 . 50
	0	Total	all	65 41 86 86 6 84 24	345 1	205 155 90 40 15	259 25 43 103 46 46	256 289 89 139	177 103 58 58 48 10 16
	atent	Ratio to prior quarter	Private physi- cian sources	0.96 1.10 (*) (*) (*) (*) (*)	1. 16 (*) 87	1.21 1.38 1.49 1.77	1.01 .71 .87 .82 (*) 1.44 1.44	1.04 1.21 1.11 .99	. 96 . 99 1. 19 . 87 . 96
Syphilis	Late and late latent	Ratio t qua	All	0. 93 1. 09 1. 39 (*) (*) (*)	1.11	1. 15 1. 22 1. 16 1. 16 1. 45	1.01 1.29 .87 .89 1.15 1.13	1.04 1.08 1.08	. 95 96 1. 02 1. 04 1. 04
	Late a	Total	all	507 95 50 211 28 91 91	6,305	4, 486 3, 624 908 593 142	2, 103 444 539 404 310 417 393	3, 662 427 1, 158 2, 077	2, 579 1, 597 926 472 217 293
	ıt	Ratio to prior quarter	Private physi- cian sources	88	1.10	1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1	(*) (*) (*) (*) 1.00 1.00 .89	. 96 . 91 1. 29 . 89	.93 .97 .97 (*)
	Early latent	Ratio t qua	Ail	1.05	. 90	1.13 1.17 1.17 1.01	1.16 1.16 1.71 1.76 1.92 1.92	. 97 1.15 92	. 92 . 94 . 84 . 73 . 88
	Ä	Total	all	189 73 88 88 3 3 3 3	2,502	1, 192 1, 126 1, 126 580 580	1,840 281 258 176 660 435 206	1, 863 239 501 1, 123	1, 254 903 611 250 27 74
	ondary	Ratio to prior quarter	Private physi- cian sources	0.88	99.	1: 08	(*) (*) (*) (*) (*) (*) (*) (*) (*)	. 88 . 87 . 69 1. 06	. 88 . 94 . 87 . 68 (*)
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Region 6—Total Alabama Florida Florida Georgia Florida Georgia Florida Georgia Florida Georgia Florida South Carolina Fuerto Rico Virgin Islands Iowa Iowa Kansas Kansas Kansas Kansas Kansas Kansas Louishana Louishana Louishana Louishana New Mexico Oklahoma Louishana	Total continental United States	Total United States, including Territories.	

FSA-PHS—Division of Venereal Disease, Office of Statistics, 7/17/50 (ML-AS)mw. Source: PHS Form 8958-B.

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Public Health Service

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948.

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 15 cents. Subscription Price: Domestic \$1.25 cents a year; foreign \$1.50

The Value of Divided Cerebrospinal Fluid Specimens¹

Richard A. Koch, M. D.2

Introduction

The two most serious manifestations of late syphilis—cardiovascular syphilis and neurosyphilis—are the two complications which continue to classify syphilis among the communicable diseases of major public health importance. Physicians, therefore, are obligated to sharpen to the ultimate degree their acuity in regard to diagnosis of these manifestations as early as possible in the course of their development.

Syphilologists generally agree that abnormalities of the cerebrospinal fluid are not pathognomonic of syphilis of the central nervous system. Only the specific serologic test approaches this designation. Moreover, other examinations of especial significance, such as cell count. estimation of protein content, and colloidal tests are frequently negative.

The source of the syphilitic reagin in the spinal fluid is not definitely known. The reagin may gain access to the fluid with protein from the blood through inflamed vessels in the meninges and choroid plexus or may be produced locally in the nervous system. However, a positive serologic test rarely occurs in the cerebrospinal fluid in the absence of neurosyphilis. A positive test may be found in cases of leprosy, frambesia, trypanosomiasis, or cerebral malaria, but these are rare in the United States. In patients with specific positive blood tests for syphilis, false-positive laboratory reports occur chiefly when reagin contains serum which is present in the cerebrospinal fluid as a contaminant because of a bloody cerebrospinal fluid puncture, a cerebral hemorrhage, or other cerebral trauma.

The Cooperative Clinical Group, in a study of 75,000 cases (1), has found asymptomatic neurosyphilis in 712 (13.5 percent) of 5,293 syphilis patients observed for more than 2 years. neurosyphilis should be suspected in a patient having latent syphilis which is diagnosed on the basis of a blood test However, because patients only reluctantly consent to one cerebrospinal fluid examination, physicians seldom secure a second such examination either to verify or to determine the diagnosis of asymptomatic neurosyphilis. Thus, irrespective of the possibility of error in laboratory technic or interpretation, a determination of the presence or absence of asymptomatic neurosyphilis is usually made on one cerebrospinal specimen handled by one laboratory and reported upon by one serologist.

The following report presents an analysis of the results obtained by sending a divided cerebrospinal fluid specimen to two official laboratories.

Statistical Analysis

Between January 1, 1941, and December 31, 1948 (a period of 8 years), the San Francisco City Clinic collected 6,954 cerebrospinal fluid specimens for analysis by three laboratories. These specimens were taken from patients who were undergoing diagnosis for syphilis or from patients who had or had not been treated for latent or late syphilis. One-third of each specimen was sent to the clinic laboratory for a differential cell count, quantitative determination of total protein, Pandy test, and colloidal gold test; one-third was sent to the laboratory of

¹ Presented at the meeting of the Venereal Disease Section, Western Branch American Public Health Association, and Western Venereal Disease Control Seminar, U. S. Public Health Service, Region X, in Portland, Oreg., on May 29, 1950.

² Chief, Division of Venereal Diseases, City and County of San Francisco Department of Public Health.

the City and County of San Francisco Department of Public Health for a Kolmer test; and one-third was sent to the laboratory of the California State Department of Public Health for a Kolmer test.

Reports were incomplete on 847 specimens because (1) the specimen was insufficient in quantity for three divisions; or (2) the laboratory reported "anticomplimentary"; or (3) one or both of the laboratories were unable to perform the test for any other reason. These tests were eliminated from the study, leaving 6,107 specimens on which this report is based.

Table 1 shows that of the 6,107 specimens examined, the 183 (3 percent) which were reported serologically positive by one laboratory and negative by another were fairly evenly distributed over the 8 years. A total of 1,042 specimens was reported positive by one or both laboratories. The 183 specimens reported positive by one laboratory and negative by the other represent 17.6 percent of the specimens reported positive by either laboratory.

The critical ratio calculated on the basis of the total specimens with one or both tests positive (1,042 specimens) is shown in table 2.

Table 1.—Results of Kolmer tests performed by two laboratories on divided samples 1 of spinal fluid at San Francisco City Clinic, January 1, 1941, to December 31, 1948

		spinal fluid les tested	with	luid samples one or both oositive		positive ar	es with one id one test
Year	Num- ber	Percent of 8-year total	Num- ber	Percent of total samples tested	Num- ber	Percent of total sam- ples tested	with one or
1941	388 490 975 850 1,080 742 778 804	6. 4 8. 0 16. 0 13. 9 17. 7 12. 1 12. 7 13. 2	69 101 184 140 150 116 138 144	17. 8 20. 6 19. 0 16. 5 13. 9 15. 6 17. 7 17. 9	13 21 24 24 29 16 30 26	3. 4 4. 3 2. 5 2. 8 2. 7 2. 2 3. 9 3. 2	18. 8 20. 8 13. 5 17. 1 19. 3 13. 8 21. 7 18. 1
Total	6, 107	100.0	1,042	17.1	183	3.0	17.6

¹ Each sample of spinal fluid was divided into three parts: one-third was sent to the Division of Laboratories of the State Department of Public Health for a Kolmer test; one-third was sent to the San Francisco City Health Department Laboratory for a Kolmer test; and one-third was retained at the San Francisco City Clinic for cell count, Pandy test, total protein determination, and colloidal gold test.

Standard error of mean percent of pooled data as the best estimate:

The critical ratio of 2.9 is statistically significant.

S. E.
$$_{\text{M}} = \pm \sqrt{\frac{(91.2)(8.8)}{1,042} + \frac{(91.2)(8.8)}{1,042}} = \pm 1.24$$

Observed difference = 3.6 percent

Critical ratio:

C. R.
$$=\frac{3.6}{1.24}=2.9$$

Table 2.—Percent positive and percent negative of total specimens with one or both tests positive

	Total specimens with one or both tests positive	Num- ber pos- itive 1	Per- cent pos- itive	Num- ber nega- tive	Per- cent nega- tive
City labora- tory State labora-	1,042	969	93. 0	73	7. 0
tory	1, 042	932	89. 4	110	10.6
Total	2, 084	1,901	91. 2	183	8.8

¹ In all tests with one test positive and one test doubtful, the doubtful test was considered positive.

Table 3.—Results of Kolmer tests on 1,042 positive divided specimeus of cerebrospinal fluid at San Francisco City Clinic

Total posi	itive spec-	Results of Kolmer tests			
Number	Percent	City laboratory	State labora- tory		
767 50 42 110 73	73. 6 4. 8 4. 0 10. 6 7. 0	Positivedo Doubtful Positivc Negative	Positive. Doubtful. Positive. Negative. Positive.		
1, 042	100.0				

Table 3 compares the city and State laboratory test results on the 1,042 positive specimens, specifically designating the degree of variation between the two laboratories. In 767 specimens (73.6 percent), both laboratories reported positive results; in 183 specimens (17.6 percent), diametrically opposite reports were made by the two laboratories; while in 92 specimens (8.8 percent), gradations of difference were reported.

Among the 183 patients with conflicting tests, these were the first tests performed for 94 (51 percent) and thus were of crucial value in alerting suspicion as to the likelihood of neurosyphilis. Thirty-seven of these cases (20.2 percent of 183) would likely not have been suspected by us, for in these instances the city laboratory report was negative. If our clinic had depended solely upon the State laboratory for reports, the diagnosis of neuro-syphilis would not have been suspected in the other 57 patients (31.1 percent of 183) with conflicting serologic results on the first test.

Table 4 shows a classification of the 183 patients with conflicting cerebro-

Table 4.—Classification of 183 patients with conflicting spinal fluid specimen reports

	Total I	Percent	negative State	Number of cases with negative city and positive State Kolmer test	Diagnosis of neurosyphilis based on—					
Line No.					Previ- ous positive Kolmer test		Clinical symp- toms	Repeat positive Kolmer test	basis of	Diagnosis other than neuro- syphilis
(1) (2) (3) (4) (5) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18)	20 26 7 3 4 20 3 9 6 4 6 2 2 3 1 1 2 1 3 1 4 4 4 6 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	11 14 4 2 2 2 11 2 5 3 3 2 3 1 1 2 7 7 7 22	12 17 3 3 14 1 1 2 1 1 1 2 1 1 1 2 1 1 2	8 9 4 3 1 6 2 3 5 3 4 1 2 1 2 1 2 1	X X X X X X	X X X X X X X X X X	X X X X X X X	X X X X X X X X	X	X X
	183	100								

Abnormal with respect to cell count, Pandy test, total protein determination, or colloidal gold findings.

spinal fluid specimen reports. An analvsis of this table reveals that patients falling within four categories likely would not have been diagnosed as having neurosyphilis if their cerebrospinal fluid specimens had been examined by one laboratory only. These four categories are: (1) patients with minimal abnormal cercbrospinal fluid findings other than serologic (line 2); (2) patients with a diagnosis of neurosyphilis confirmed by repeated positive Kolmer tests (line 4); (3) patients with minimal abnormal cerebrospinal fluid findings other than serologic and repeated positive Kolmer tests (line 9); and (4) patients diagnosed solely on the basis of positive Kolmer tests (line 16). These number 48 patients. As these 48 patients were diagnosed as having neurosyphilis because their cerebrospinal fluid specimens were examined by two laboratories, one might postulate that approximately onehalf of these would have been missed if their cerebrospinal fluid specimens were examined by one laboratory only. Thus out of these 48 patients, it seems fair to postulate that one-half (13.1 percent of the total 183 patients) were diagnosed only as a result of divided cerebrospinal fluid examinations.

Summary

- 1. An analysis is presented of the reports on 6,107 cerebrospinal fluid specimens each sent to two official laboratories.
- 2. There were 1,042 cerebrospinal specimens returned with conflicting serologic reports. Detailed analysis of the variations in these reports is made.
- 3. It is estimated that about 24 patients would not have been diagnosed as having neurosyphilis had not divided specimens been secured.

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The Treatment of Syphilis of the Masses

R. R. Willcox, M. B.1

During 1949 I was fortunate enough to make not only a venereal disease survey throughout Southern Rhodesia but also (apart from brief visits to hospitals in parts of Northern Rhodesia and Portuguese East Africa) to study vencreal disease problems at first hand in the Union of South Africa, Egypt, Turkey, Syria, Lebanon, East and West Pakistan, and Iraq. Attention was constantly

focused during this time on problems of syphilis of the masses. The venereologic enlightenment encountered was sometimes slight, often prepenicillin, and occasionally prearsphenamine.

Two impressions which have emerged in greater relief than the rest are: (1) syphilis as a nonvenereal complaint is much more common than is generally realized; and (2) since the evolution of simplified, effective treatment for venereal syphilis has quite outstripped the installation of proper diagnostic facilities, modern treatment will, in general, have to be applied in spite of this limitation.

¹ Physician in Charge, Venereal Diseases Department, King Edward VII Hospital, Windsor, England: Consultant Senior Assistant, Venereal Diseases Department, St. Mary's Hospital, Paddington, London, England.

Extravenereal Syphilis

Quite apart from yaws, which affects millions throughout the tropical belt of the world, and pinta, which also affects a very large number of persons in the Western Hemisphere (both of which disorders are often considered to be separate from syphilis, although some, e. g., Hudson, postulate that they are caused by the same organism, *Treponema pallidum*), there are other diseases of an intermediate nature which have also been described. One of these is the bejel of the Euphrates Arab, first described by Hudson (1) in 1928 and considered to be a local form of treponematosis.

It is said that a million persons in Iraq may be affected by bejel, which affects primarily the children. disease has no primary stage although Akrawi (2) found that a typical chancre was produced in the experimental infection of man. The usual clinical signs are of the secondary type, with genital and perianal condylomata, genital and oral mucous patches, split papules at the angles of the mouth, bone pains, and laryngitis. Later complications are usually gummatous (particularly of the soft palate, nasal septum, bones, and soft tissues). The disease is spread by close contact in conditions of filth, flies, and overcrowding.

While in Southern Rhodesia I encountered, among the Karanga people in the southern part, a disease locally called njovera, which primarily affects children and manifests itself by anogenital condylomata, mucous patches in the mouth, and split papules at the commissures of the lips. Organisms resembling T. pallidum may be found by darkfield illumination, and the serum tests for syphilis are positive. Late complications include gangosa-like lesions (which are also given the name "njovera") and gummata of the palate and other sites. No primary sores were observed in the children but an occasional "throw-back" was seen as a nipple chancre in the mother of a breastfed infected child. Although people of these parts also call the conventional

syphilis of the towns by the word "njovera," they undoubtedly distinguish between the venereal and the nonvenereal form. At that time I (3) believed that njovera was indeed syphilis and was similar to the bejel of the Euphrates Arab which I had not then seen. Later that year I observed bejel in the Ramadi Liwa of Iraq and found no reason to change my opinion (4).

It is considered unlikely that such manifestations of syphilis are confined to this part of Africa alone, for the Dark Continent is still medically unexplored. Indeed, in Southern Rhodesia the disease was found to extend beyond the limits covered by the tribes mentioned, where it was called by other names. Hearsay evidence appeared to indicate its prevalence in Bechuanaland. Manson-Bahr (5) refers to a possibly similar condition in East Africa, while extravenereal syphilis has been endemic for years in the Balkans, and it is considered possible, from reports, that it is present also in Afghanistan. It certainly has existed within a reasonable time in Scandinavia (radesyge) and probably still exists to a lesser degree in History also tells us of the sibbens of Scotland and of a similar condition encountered during the early settlement of Canada.

Hudson (6) believes that the spread of the disease is due to close nonvenereal contact, aided by filth, flies, and conditions of overcrowding. A definite increase in extravenereal syphilis of children was noted in postwar Budapest by Féjer (7). During the years 1937–39 only 3 examples were noted in the clinic there, while in the years 1945-47 the number had increased to 30, only 3 of which had primary sores. In Chicago, in 1947, 20 cases of asexual syphilis in children were noted by Eisenberg et al. (8). In these American cases, as in bejel and njovera, there was again an absence of the primary stage, and overcrowding was believed to have been responsible.

Thus, whatever the final verdict as to the relationship of yaws and pinta to syphilis (there appears to be some justification for giving these diseases separate labels, although the in vitro immobilization test of Nelson and Mayer (9) may nelp in deciding), Hudson's theory as to the relationship of syphilis to the extravenereal forms, such as bejel, gain considerable support from the random observations from Southern Rhodesia, Chicago, and Budapest.

Extravenereal syphilis is therefore a not uncommon event in some of the less civilized and poorer populations of the globe—in some respects, a reverse of the adage that "civilization brings syphilization." It is spread by close contact and possibly also by flies, which flourish under conditions of squalor. Syphilis prevention thus becomes in part the question of the provision of proper housing and sanitary amenities, for if unsatisfactory hygienic conditions are allowed to continue, any mass campaign based on penicillin is likely to be only temporarily successful. Indeed, should it be proved that flies are a common method of transference, it might be that under certain circumstances DDT would be more effective than PAM! However, as the "provision of amenities" means but little to the raw native in the bush, the whole matter becomes fundamentally one of racial progress. As such progress is achieved, extravenereal syphilis is then exchanged for venereal syphilis, for which penicillin remains the best weapon.

Venereal Syphilis

There are two concepts of the mass approach: (1) to treat the entire population of a given area by a sterilizing dose of penicillin, aimed primarily not at curing the individual but rather at reducing the common infectious pool (experiments of this nature in both yaws and syphilis are being undertaken by the World Health Organization in several parts of the world); and (2) to treat all persons clinically suspicious (this method needs must include persons with chancroid, lymphogranuloma venereum, and granuloma inguinale, for, under existing

conditions, diagnosis is often made by relatively inexperienced personnel).

In many clinics in the countries visited, all patients are not necessarily seen by a doctor; cases of genital discharge tend to be labeled "gonorrhea" and cases of penile or near genital sores, "syphilis." Often darkfield illumination is unavailable and follow-up is impossible for all but a few In the past, the standard individuals. treatment has been a few injections of arsphenamines with or without bismuth, since prolonged hospitalization has been impracticable. Owing to the absence of proper diagnostic facilities, such treatment has been given to all patients with genital sores. The acceptance of this concept, however realistic, has led to an unsatisfactory management of venereal disease therapy and has delayed provision of proper diagnostic facilities to the peoples concerned. It must be said, however, in fairness to the medical officers concerned, that venereal disease problems are only a small fraction of the many problems encountered, although the diagnostic situation could have been bettered by the proper training of technicians.

Now that the treatment of syphilis has become so simple, it has quite outstripped the simplicity of diagnosis. Therefore, rather than deny millions the benefit of mass treatment pending the years which must elapse (before the medical officers and orderlies situated in the remoter parts of Africa and other places can master accurate diagnosis by darkfield examination and serum tests), one must prepare for the application of modern treatment in advance of such diagnostic aids.

Procaine Penicillin With Aluminum Monostearate

Secondary syphilis in primitive people may usually be diagnosed with reasonable certainty by the naked eye; it is in cases of penile sore that most trouble is experienced. Chancroid is almost universal in such individuals and is often treated as for syphilis, frequently by an

inadequate course of neoarsphenamine. Whether inadequacy is deliberate or brought about by default the result is the same.

That such treatment for syphilis is inferior to penicillin will not be denied. The single-shot method employing 2.4 mega units of procaine penicillin with 2 percent aluminum monostearate would appear to be the ideal for these races. Initial reports by Thomas et al. (10) and the more recent summing-up by Bauer et al. (11) suggest that the results obtained by such treatment are not inferior to those obtained with penicillin in oil and beeswax, given over 8 days and involving double the amount (and therefore double the cost) of penicillin.

Realizing that, in applying such treatment to syphilis of the masses, chancroid and lymphogranuloma venereum would also have to be included, the author has recently tried to establish two points: (1) that the routine administration of six to eight weekly or biweekly injections of neoarsphenamine in all cases of penile sore is a bad treatment for chancroid (it being taken for granted that it is inferior to penicillin for syphilis); and (2) that the single-shot treatment with PAM is fairly adequate for the majority of cases of soft sore—at least throwing recalcitrant cases into relief so that sulfonamides may be superadded.

The first point was proved by work on the experimental infection of man, the results indicating that no grounds for complacency exist for those who still consider neoarsphenamine to be a fairly effective antichancroidal drug and who recommend its use for all cases of penile sore. If the second point could be proved, the mass treatment of all cases of penile sore by the one drug (PAM), without darkfield examination or serologic diagnosis, is then free of medical objections as regards the patient, in situations in which follow-up is impossible. The single-shot treatment with PAM was therefore given to a representative group of African Negroes with penile sores, including chancroid.

Single-Shot Treatment With PAM in Experimental Chancroid

If 0.05 ee. of bubo fluid from an untreated individual is injected intradermally into a patient, or into another untreated volunteer, within 24-48 hours a papule develops which (within 48-72 hours) becomes a pustule, and, if treatment is still withheld, proceeds to chancroidal ulceration. If, however, the recipient is treated from the time of inoculation with effective drugs no such reaction will occur. By this method the relative effectiveness of different drugs may be compared, the experiments being controlled by observation of a few untreated volunteers. Analternative method is to treat the patient with the chancroidal bubo with one of the drugs to be tested, and to inject the bubo fluid into other individuals 24 hours later after the onset of treatment to ascertain whether or not the bubo fluid has lost its virulence, which it does within 24 hours if effective drugs are used.

Such methods were employed by the author (12, 13, 14) during 1949. results showed that antimony, bismuth, and neoarsphenamine were ineffective prophylactics against experimental chancroid (25 "takes" out of 38 in the neoarsphenamine-treated series), whereas sulfonamides, streptomycin, aureomycin, chloramphenicol were Penicillin in eight daily injections of an oil-beeswax mixture was also 100-percent effective in 32 recipients. Experiments with the single-shot treatment employing procaine penicillin G in oil with 2 percent aluminum monostearate gave interesting results. Detectable levels of penicillin in the blood were found on each of 9 days following single injections of 2.4 mega units of this preparation (15). It was found, however, that if the interval between the penicillin injection and the inoculation with chancroidal material was within 0-4 days, there were only 2 "takes" in 10 persons, whereas if the interval was 5-8 days (the serum level. although still present, being of a smaller

degree and sustained for a shorter time), the results were much less successful, there being 7 "takes" in 11 persons.

From these experiments it may be inferred not only that neoarsphenamine is relatively ineffective against chancroid but also that penicillin in adequate doses has a definite curative effect. However, in lesser amounts, producing a lower blood level sustained for a shorter time, its action is much less certain. It is considered likely that the single-shot treatment of syphilis employing 2.4 mega units of PAM will benefit the majority of cases of soft sore even if it is not 100-percent successful.

Trials of Single-Shot Treatments With PAM on African Negroes With Genital Sores

To test this hypothesis, single injections of 2.4 mega units of PAM were given indiscriminately to a number of individuals with penile sores in Salisbury, Southern Rhodesia. Three daily darkfield examinations and serologic tests for syphilis were performed before treatment.

Thirty patients had darkfield-positive early syphilis, and the sores healed, on an average, in 6.36 days (longest, 14 days); 22 had darkfield-negative, sero-positive, clinical early syphilis, and the sores healed, on an average, in 8.27 days (longest, 18 days); 23 had darkfield-negative, seronegative, clinical primary syphilis, and the sores healed, on an average, in 6.45 days (longest, 13 days); in 5 patients who had negative darkfield clinical early syphilis, in whom there was no record of the serology, the sores healed, on an average, in 5.8 days.

Of these 80 early syphilis patients, many must have had a double infection with soft sore. Mixed infection was very common, and the occurrence of suppurating buboes in patients with darkfield-positive early syphilis was no rarity. Indeed, earlier in the investigation at this same clinic, 570 smears from 243 genital sores were examined for Ducrey's bacil-

lus. Organisms morphologically resembling Hemophilus ducreyi were found in 257 instances among 144 patients. Diagnoses of the positive cases were as follows: Soft sore, 75; primary syphilis, 65; other, 4. The Dmelcos skin test (Ito reaction) performed on 290 males with venereal diseases, taken at random from the same clinic, gave 129 positive results. Yet, in spite of this, of the 80 early syphilis patients treated with PAM, only 12 required additional therapy (oral sulfadiazine in 8 and calomel ointment in 4).

Nineteen cases of clinical soft sore were also treated. The majority had typical multiple sores, and 7 had fluctuant buboes. Repeated daily darkfield examinations were negative in all cases, and the serum tests for syphilis were negative in 15 and positive in 4. All patients received single injections of 2.4 mega units of PAM and were ready for discharge from the hospital, on an average, in 5.5 days (longest, 13 days), buboes being aspirated as required. Three were regarded as failures and required oral sulfadiazine.

Lymphogranuloma venereum, common in Africa, tends to be grouped with syphilis; therefore to be allowed for is the fact that such cases also would receive routine treatment with PAM. Several years ago, when working in West Africa, the writer (16) treated 25 Gold Coast Africans and 2 Europeans suffering from climatic bubo with what today would be regarded as very small doses of penicillin. Seventeen cleared up without further therapy. During the present investigation, four such cases were treated with single injections of 2.4 mega units of PAM; one proceeded to fluctuation and was aspirated, but all were discharged from the hospital in an average of 7 days.

The results of these tests are encouraging and indicate that as soon as the single-shot treatment has been definitely proved to be reasonably effective for early syphilis, it will be medically sound to administer it for all forms of penile sore in African and other such populations, with the proviso that sulfonamide

drugs be held in readiness for the few resistant cases of chancroid and for lymphogranuloma venereum. The residue will then consist largely of granuloma inguinale.

However, it is necessary that the dose of PAM in one injection should be not less than 2.4 mega units, for less than this is relatively ineffective in soft sore. While experiments with mass treatment in both yaws and syphilis have sometimes employed lesser amounts, it appears undesirable not to employ a curative dose (2.4 mega units) rather than a prophylactic dose (300,000–600,000 units) for all persons showing clinical signs of infection, reserving the smaller dose for symptomless contacts discovered in the epidemiologic dragnet or for members of population groups under random consideration.

Oral Antibiotics

Aureomycin and chloramphenicol have some action upon syphilis and soft sore. Although Wetherbee et al. (17) considered that aureomycin has only a transient inhibitory effect against H. ducreyi in vitro, personal experience in experimental infection and the first case reports by Zheutlin and Robinson (18) and by Greenblatt et al. (19) tell a different story. It may be that these drugs, on account of their ease of administration, will one day be used in the mass treatment of populations of countries such as those visited, but the necessity of repeated doses denies them the supreme advantage possessed by the single-shot treatment with penicillin. It is worth noting in this respect that Ampofo and Findlay (20) have employed oral aureomycin in the Gold Coast to good effect in both yaws and tropical ulcer. They state, however, that in order to placate African suspicion of any treatment not involving an injection, 2 cc. of saline solution was administered intramuscularly with each oral dose.

While this viewpoint deserves consideration, supported as it is by persons highly experienced in African medicine, in my opinion, it should be examined with

care. I, too, was faced with a shibboleth when switching from arsenicals to penicillin. The African, I was frequently informed, preferred an intravenous injecof neoarsphenamine, which alleged to have aphrodisiacal properties and would "increase his power"; he would therefore never accept intramuscular penicillin as a substitute. This method was tested, however, and there were no complaints from many hundreds treated The African apunder my supervision. preciated the previously unknown rapidity of healing of lesions, a fact equally evident in the smaller numbers treated with the oral antibiotics. It is felt that one should give the treatment which is medically the most propitious and let the results speak for themselves. The grain of truth in this observation concerning neoarsphenamine has become magnified into a mound of falsehood and it is often put forward by those who resent the present day rapid treatment of syphilis as making immorality easier. African prejudice in regard to the oral antibiotics may have to be considered, but we must await the results of large-scale trial first.

Summary and Conclusions

- 1. The widespread distribution of extravenereal syphilis is noted. Another local variety, the njovera of Southern Rhodesia, is described.
- 2. The value of the single-shot treatment of syphilis employing PAM for primitive peoples with venereal and extravenereal syphilis is stressed. The administrative advantages of a single injection in territories which are visited only occasionally by a doctor and in which proper follow-up is impossible are enormous, and precautions against misuse of the penicillin in the absence of the doctor are easier to observe.
- 3. The difficulties under existing conditions of proper diagnosis backed by pathologic support are emphasized, and the feasibility of giving one-shot treatment with PAM to all is considered.
- 4. Of 99 African Negroes with penile sores given single intramuscular injec-

tions of 2.4 mega units of PAM, only 11 required sulfa drugs in addition.

- 5. The value of penicillin and of sulfonamides, aureomycin, and chloramphenicol in adequate doses for the treatment of chancroid, and the inadequacy of neoarsphenamine, were indicated by experimental inoculations.
- 6. It is considered that single injections of PAM given to Africans with sores should consist of not less than 2.4 mega units, for less than this amount is insufficient for chancroid.
- 7. The African does not mind substituting the more effective intramuscular injection of penicillin for intravenous neoarsphenamine.
- 8. A study has been made of conditions as they exist 45 years after the discovery of *T. pallidum*, in countries where many doctors treating venereal disease patients still have difficulty in confirming diagnosis. An attempt has been made to face medical limitations without condoning them and to make a realistic approach to the problem of venereal disease treatment until such time as they can be rectified.

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Treatment of Gonorrhea With Chloramphenicol (Chloromycetin)¹

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The use of chloramphenicol (Chloromycetin) for the treatment of gonorrhea was first reported by Smadel and associates (1, 2). Subsequent reports have been presented by Greenblatt and coworkers (3, 4) and by Robinson and Robinson (5).

These reports have shown that Chloromycetin, in relatively large single or multiple doses, is effective for the treatment of gonorrhea. An investigation of the effectiveness of small single doses seemed indicated.

Clinical Data

Males with acute gonorrheal urethritis in whom the gonococcus could be demonstrated by spread and culture were selected for study. All cultures were controlled by study of morphology and of sugar fermentation of the organisms. Criteria of cure were the disappearance of symptoms and three negative spreads and cultures over a period of 7 to 10 days. The study included 96 males. Twentysix patients did not complete the followup to establish cure. Table 1 shows the results of treatment with 750 mg, or lesser amounts of Chloromycetin given as a single oral dose. In computing the cure rate it was assumed that the same percentage of cures would occur in patients not observed as in those observed.

The clinical progress of patients was similar to that seen after penicillin treatment. In all patients, including those in whom failures later became evident, the discharge ceased at 24 hours or was replaced by a thin, watery secretion. How-

Table 1.—Results of treatment of gonorrhea with 750 mg, or lesser amounts of Chloromycetin given as a single oral dose

Posage	Total number of cases	Number of cases with fol- low-up	Number cured	Percent cured
750 mg	75	50	48	96. 0
500 mg	16	16	12	75. 0
250 mg	5	4	1	25. 0

ever, in some cases the discharge which reappeared after 2 to 3 days became purulent, and gonococci could again be demonstrated.

Spreads from the discharge of 16 patients, treated with 500 mg. of Chloromycetin, were examined hourly for 6 hours. Generally, at the first and second examinations, no appreciable change in appearance of the spread was seen. the 3-hour examination the gonococci appeared swollen; in 4 hours only a few extracellular organisms were visible. The leucocytes which had been clearly outlined in earlier spreads began to show crenation or ruptured cell membranes, fragmentation, eccentricity or extrusion of the nucleus, granular cytoplasm, and less affinity for the counterstain. After 5 hours, only an occasional diplococcus was seen intercellularly, and at the end of 6 hours, no organisms were found. In cases which were not cured, it appears that concentration of the antibiotic to which some organisms were exposed was bacteriostatic instead of bacteriocidal and that recovery of these organisms had taken place.

Since workers from our group have shown in a previous report (6) that Chloromycetin has an antitreponemal effect against *Treponema pallidum*, there may be some danger of masking syphilis

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when Chloromycetin is used to treat gonorrhea. In three patients a single oral dose of 250 mg. was not effective in clearing primary or secondary lesions of their syphilis organisms. A single oral dose of 500 mg. caused the organisms to disappear in one of two patients at 48 hours; in the other patient the organisms were demonstrable at 96 hours.

In our opinion, the danger of masking syphilis by a dose of 750 mg. of Chloromycetin for gonorrhea is about the same as after treatment with penicillin.

Comment

No toxic or allergic reactions were observed in 96 patients after treatment with 250 mg. to 750 mg. of Chloromycetin. The oral use of Chloromycetin for the treatment of gonorrhea is acceptable to patients and is suitable for office or clinic administration.

Conclusions

- 1. Chloromycetin is an effective drug for the treatment of gonorrhea. Ninetysix percent of 50 patients were cured with a single oral dose of 750 mg. of Chloromycetin. However, results with 500 mg. and 250 mg. do not appear to be satisfactory.
- 2. Chloromycetin has not produced toxic reactions in the dosage used for the treatment of gonorrhea.
- 3. Patients treated with Chloromycetin for gonorrhea should have the same 3 to 6 months' posttreatment observation as

has been advised following penicillin treatment. The same potential danger of masking syphilis exists as after penicillin treatment.

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Gonococci and the Menstrual Cycle¹

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The postmenstrual phase is generally considered the most favorable one for the demonstration of gonococci in the cervix, as stated by Buschke and Langer (1), Marshall (2), Pelouze (3), Lomholt (4), and Zieler and Siebert (5). Naujoks (6) maintains that menstruation is a better provocative than Arthigon or Aolan. Frank (7), however, made a microscopic study of the number of gonococci in the cervix before and after menstruation and found that they increased in 16 percent of the cases and decreased in 13 percent but remained unchanged in 71 percent. Joachimovits (8) and Franz (9) found the premenstrual phase favorable for the demonstration of gonococci, the latter even recommending the menstrual period.

An interesting study of this question was made by Koch (10). She examined smears and cultures from the cervices of 50 patients who had normal menstrual cycles and who were suspected of having acute gonorrhea. Cervical hydrogen ion (pH) determinations were made. Positive cultures were obtained in 35 cases, and in these the pH of the mucus was 6.8 or more. Half of the negative cultures were obtained during the postovulatory or luteal phase, and the pH range of the cervical mucus was from 5.2 to 6.6.

Koch's study included six untreated patients with bacteriologically proved cervical gonorrhea who were hospitalized for the period of their current cycles and for part of their subsequent cycles. Daily smears, cultures, and pH determinations were made from the cervical mucus. The pH curve was considered normal in 4 of the 6 cases. Of the 78 cultures obtained from these 4 cases, 54 were positive.

Koch also observed that the gonococcus in vitro was inhibited by pure crystalline progesterone in a concentration of 1 to 20,000 but was not inhibited by pure crystalline alpha estradiol, even in a concentration of 1 to 5,000. She concluded that positive cultures are associated with the estrogenic phase and negative cultures with the latter part of the luteal phase, the cervical mucus then being most acid and progesterone activity at its height.

From the Women's Clinic in Malmo, Bergqvist (11) collected 39 cases in which the dates of cervical cultures positive for the gonococcus could be correlated with days of the menstrual cycle. Thirty-three of the cases (84.6 percent) were cultured during the estrogenic phase and 5 (12.8 percent) on the twenty-second to the twenty-fifth days of the cycle, when it is claimed that a secondary rise in the estrogens occurs. Bergqvist considered that his results supported those of Koch.

Between 1946 and 1949 we have compiled material from the Kumpula State Hospital that throws additional light on the part played by the menstrual cycle in the demonstration of cervical gonorrhea.

Material

We selected 343 cases of cervical gonorrhea in which the date of menstruation was known from the past history, from the temperature chart, or from both sources. Of these patients, 222 had concurrent urethritis, and a few had proctitis also. In addition, some of the patients suffered from involvement of the uterine adnexa.

Forty-nine (90.7 percent) were taken during the estrogenic phase or during the first 2 days of the luteal phase, and the pH was 6.8 or more. Of the 24 negative cultures, 17 (70.8 percent) were obtained during the luteal phase, and the pH ranged from 5.8 to 6.5.

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² Director.

The diagnosis of gonorrhea was made in every case by positive smear, positive culture, or both. Cultures were made in the Department of Serology and Bacteriology of the University of Helsinki and later in the State Serum Institute. Either the McLeod-Reymann or the Engelson medium was used. As a rule, treatment was started not on the basis of one positive finding but only after examinations repeated a few times at intervals of from 3 to 4 days. The diagnosis of cervicitis in 235 patients was based on at least two positive findings. Smear and culture were both positive at least once in 234 patients. In 39 cases the diagnosis was based on two or more positive cultures, in 37 cases on only one positive culture, in 10 cases on two or more positive smears, and in 23 cases on only one positive smear.

Eight hundred and seven examinations that included both smears and cultures were made, and the findings are shown in table 1. The 807 cervical specimens yielded 394 positive smears (48.8 percent) and 560 positive cultures (69.4 percent), the ratio of positive smears to positive cultures being 1 to 1.4. This ratio is

Table 1.—Smear and culture findings resulting from 807 examinations for gonorrhea

Findings	Number	Percent
Both smear and culture positive_ Smear negative, culture positive_ Smear positive, culture negative_ Both smear and culture negative_ Total	121	33. 8 35. 6 15. 0 15. 6

lower than that found by many observers and may be due to careful microscopy, to the mediums used, or to the fact that our cases were all untreated. Our incidence of positive cultures is the same as in Koch's 4 cases, in which 69 percent of 78 cultures were positive.

Demonstration of Gonococci During the Different Phases of the Menstrual Cycle

The bacteriologic examinations were divided into two groups on the basis of

knowledge of the date of onset of menstruation: (1) before examination and (2) after examination. The first group included 608 specimens and the second group 511. Some overlapping was present because in 312 examinations the dates of onset of both the current and subsequent cycles were known, and these specimens are therefore in both groups.

Tables 2 and 3 show the distribution of the results with smears and cultures over the successive phases of the menstrual cycle. Table 2 is calculated forward from the preceding or current menstruation, and table 3 is calculated backward from the onset of the subsequent men-

Table 2.—Results of bacteriologic examinations during different phases of the menstrual cycle calculated forward from the onset of the preceding or the current menstruation

	cle	exam- ns	Posi sme		Positive cultures		
Phase of cycle	Days of cycle	Number of exam inations	Number	Percent	Number	Percent	
Menstrual	1-5 6-11 12-16 17-25 26-	151 143 89 116 109	90 75 52 48 54	59. 6 52. 4 58. 4 41. 4 49. 5	97 99 61 80 76	64. 2 69. 2 68. 5 69. 0 69. 7	
Total		608	319	52. 6	413	68. 0	

Table 3.—Results of bacteriologic examinations during different phases of the menstrual period calculated backward from the onset of the subsequent menstruation

	cle	exam- ns		itive cars	Positive cultures		
Phase of cycle	Days of cycle	Number of exam inations	Number	Percent	Number	Percent	
Uncertain Postmenstrual_ Ovulatory Postovulatory_ Premenstrual	6-11 12-16 17-25 26-28	63 117 97 157 • 77	28 59 46 72 28	44. 4 50. 4 47. 4 45. 9 36. 4	44 83 67 114 54	69. 8 70. 9 69. 1 72. 6 70. 1	
Total		511	233	45. 6	362	70. 9	

struation. The division into phases cannot be quite exact, because the material includes both short and long cycles and, evidently, anovulatory cycles also. division is most reliable near the onset of a known menstruation but becomes increasingly uncertain further from it. According to present opinion, the shortening or lengthening of the cycle occurs in its first part, that is, during the estrogenic phase. If this is so, the phases can be more accurately determined backward from a menstruation than forward. In that case the data in table 3 are more reliable than those in table 2, since the date of onset of menstruation recorded during hospitalization is more accurate than that of the preceding cycle, for which the memory of the patient has to be used.

Cultures

With regard to cultures, both tables show a great uniformity of the results during the different phases of the menstrual cycle. The positive cultures were so evenly distributed that their percentages varied, with one exception, only from 68.5 to 72.6. That exception was noted during the menstrual period, when the incidence of positive cultures was 64.2 percent. This difference is not statistically significant.

Smears

The results of the smear examinations were less uniformly distributed than those of the cultures. As shown in table 2, the time of menstruation was the most favorable for smear examinations, 59.6 percent having been positive at this time. The somewhat less favorable results during the postmenstrual and ovulatory phases may have been due to chance The postovulatory phase, however, yielded almost 20 percent fewer positive smears than were obtained during menstruation, and the difference is statistically significant, since Chi square equals 8.72 and P equals 0.003. The poorest result was during the premenstrual period, in which only 36.4 percent of the smear examinations were positive. The difference between this phase and the time of menstruation is even more significant (Chi square equals 11.03 and P equals 0.001) than the difference between the time of menstruation and the postovulatory phase. Further back from the onset of menstruation, the incidence of positive smears increases gradually, being 45.9 percent during the postovulatory phase, 47.4 percent during the ovulatory phase, and 50.4 percent during the postmenstrual phase.

The incidence of positive smears during the same phases of the cycle differs slightly in the two tables, probably because in table 2 the division into phases is forward from the remembered onset of menstruation and in table 3 backward recorded onset. As already from a stated, variations in the length of the cycles render this division into phases increasingly uncertain as the distance from a known menstruation increases, and this uncertainty affects different phases in the two tables. Because of this increasing uncertainty, we have classified as uncertain those bacteriologic examinations that were more than four phases from the onset of menstruation, although their results are included in the table for the sake of completeness.

Conclusions and Discussion

Our results show clearly that the phase of the menstrual cycle is not of importance in the demonstration of gonococci from the cervix by culture, since the incidence of positive cultures was about the same—around 70 percent—during all phases. On the other hand, the incidence of positive smears was highest—59.6 percent—during menstruation and almost as high during the whole estrogenic phase. During the luteal phase the results were significantly less good, and the lowest incidence of positive smears—36.4 percent—occurred during the last 3 days preceding menstruation.

These results have been checked by a study of the findings in the 234 cases in

which diagnosis was based on both smears and cultures. Although this reduction of the material changed the percentages of positive findings to some extent, there was no significant change in the proportion of positive examinations, either smears or cultures, during the different phases.

In regard to smears, our study confirms previous opinions that the postmenstrual phase is more favorable than the premenstrual period for the demonstration of gonococci. However, in regard to cultures, no such difference can be observed, and we have therefore been unable to confirm the findings of Koch (10) and of Bergqvist (11). Both of these series, however, were small. In one series Koch compared 50 bacteriologic examinations, 35 of which were positive and 15 negative. It was not known whether or not the patients with negative cultures had gonorrhea. Two of the six patients in her smaller series were excluded, thereby greatly altering the percentages of positive cultures during the different phases. Bergqvist's 39 positive cultures were all from different patients, and their distribution over the menstrual cycle depends essentially on when the patients applied for medical attention. It should be remembered that patients often refrain from consultation during menstruation, with the result that examinations tend to accumulate during the postmenstrual phase. The fact that involvement of the fallopian tubes often occurs in connection with menstruation increases this trend. This may be a simple explanation of the fact that 33 of Bergqvist's cultures were obtained during the estrogenic phase.

It would be of interest to know why the results of smear examinations vary during the different phases of the cycle. The uniformity of the culture results indicates that variability of the microscopic findings may be due to some secondary factor. One explanation might be the decrease in mucous secretion at the end of the luteal phase and the resulting difficulty in making satisfactory smears. Similar variations in the leucocyte counts

would also bias the results. Smears rich in leucocytes are often examined longer than those in which the leucocytes are rare. However, analysis of our cases in regard to this possibility revealed no distinct trend.

Summary

The authors have studied the effect of the different phases of the menstrual cycle on the demonstration of gonococci in the cervix. An analysis was made of 807 smears and cultures obtained prior to treatment from 343 patients hospitalized because of gonorrheal cervicitis. Positive smears totaled 394 (48.7 percent). Positive cultures totaled 560 (69.4 percent). The onset of menstruation was known in relation to 608 examinations and the onset of the subsequent menstruation in 511.

No significant variation of positive cultures in relation to the day of the menstrual cycle was found, the incidence of positive cultures varying only slightly on either side of 69.4 percent.

Some variation was observed in the smear examinations. The positive smears were highest (59.6 percent) during menstruation. The percentage during the rest of the estrogenic phase was slightly lower. Significant decreases in the number of positive smears were obtained during the luteal and premenstrual phases, the lowest (36.4 percent) being obtained with the latter.

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CURRENT NOTES AND REPORTS

Kentucky Intensifies Search for Syphilitic Children

A five-point drive against congenital syphilis in nine Kentucky counties was launched in July.

As outlined in "News and Plans of the Kentucky State Department of Health," the program is aimed at finding and referring for treatment cases of congenital syphilis. The plan calls for: (1) reexamination of all known cases of syphilis among women of child-bearing ages; (2) examination of all children born to such women since the onset of their in-

fection; (3) blood test for syphilis in preschool and school examination; (4) blood testing all women who, according to their babies' birth certificates, had no prenatal blood test; and (5) reexamination of all cases of late syphilis.

Aided in the case-finding program by a grant of money and personnel from the United States Public Health Service, the program is scheduled to begin in Bell, Harlan, Letcher, Pike, Floyd, Knott, Perry, Leslie, and Clay Counties.

CURRENT LITERATURE

AM. J. M. TECHNOL., HOUSTON

A bacteriological study of urethritis following penicillin therapy of gonorrhea. Ruth
 A. Kirby, Matthew A. Bucca, and J. D. Thayer. Am. J. M. Technol., 16: 113–119, May 1950.

The results of bacteriologic study of 96 patients with urethritis at the United States Marine Hospital, Staten Island, are presented. The predominant organisms found were staphylococci and diphtheroids. No single entity was found to be the cause.

AM. J. OBST. & GYNEC., ST. LOUIS

Chloromycetin in the therapy of granuloma inguinale. Robert B. Greenblatt, Virgene S. Wammock, Robert B. Dienst, and Robert M. West. Am. J. Obst. & Gynec., 59: 1129-1133, May 1950.

Between March and September 1949, Chloromycetin was effectively used in 23 women patients at the University of Georgia Hospital. Six case histories are presented. From experience it appeared that the ideal dosage was 500 mg. every 6 hours for 10 to 20 days. If healing is incomplete, therapy should be continued until 50 to 70 gm. are given. Donovan bodies in most instances disappeared in 2 to 4 days.

AM. J. PUB. HEALTH, NEW YORK

Role of case finding in syphilis control today. Johu J. Wright and Cecil G. Sheps. Am. J. Pub. Health, 40: 844-849, July 1950.

Of the three major case-finding methods (contact investigation, education, and serologic screening), serologic screening procedures are the least effective and not to be relied upon for controlling the spread of the disease. More is accomplished through education with males than with females. In the female, infectious syphilis contact investigation is the most important case-finding measure.

The status of venereal disease control. Editorials, Am. J. Pub. Health, 40: 864-866, July 1950.

Even though there is a decrease in rates, there remain areas where case-finding and reporting systems are poor and venereal disease continues undiscovered. There is a possibility that undiscovered cases of syphilis are partially responsible for the constant level of congenital syphilis morbidity. Every case of congenital syphilis is a failure of syphilis control. Leaders of the control program must give thought to improvement of early detection, and health administrators must not be lulled by the decrease of reported cases.

AM. J. TROP. MED., BALTIMORE

Complement fixation studies in granuloma inguinale. Henry Packer and Julius Goldberg. Am. J. Trop. Med., 30: 387-395, May 1950.

The serologic characteristics of *Donovania granulomatis*, with special reference to antigens which it has in common with members of the tribe Eschericheae, were studied employing the serums of rabbits immunized against these organisms. Since organisms differing in taxonomic position share common antigens, there did not appear to be sufficient grounds for changing the taxonomic posi-

tion of *D. granulomatis* to bring it closer to organisms to which it showed a serologic relationship.

ANN. ALLERGY, ST. PAUL

Hypo-allergic penicillin. S. William Simon. Ann. Allergy, 8:194-201, 289, Mar.-Apr. 1950.

Three syphilitic patients with histories of previous reactions to penicillin were given Decapryn-penicillin (100,000 units penicillin plus 5 mg. Decapryn succinate dissolved in normal saline). All took the entire course of 9,000,000 units without reaction and with good therapeutic response.

ARCH. DERMAT. & SYPH., CHICAGO

Lupus erythematosus: serologic and chemical aspects. Charles R. Rein and George H. Kostant. Arch. Dermat. & Syph., 61: 898-903, June 1950.

The problem of biologic false-positive reactions in the serologic test for syphilis in lupus erythematosus is discussed. Serologic tests for syphilis performed on 178 serums of patients with lupus erythematosus revealed an over-all incidence of 35 percent for biologic false-positive reactions.

Granular cell myoblastoma. Report of a case simulating granuloma inguinale. Arthur B. Kern, Jerome J. Kaufman, and Frank C. Combes. Arch. Dermat. & Syph., 62: 109–116, July 1950.

Patient was a 25-year-old Negro woman complaining of lesion on her thigh. Clinical appearance was suggestive of granuloma inguinale, but attempts to demonstrate Donovan bodies were unsuccessful.

ARCH. INT. MED., CHICAGO

Syphilis. A review of the recent literature. Herman Beerman, Leslie Nicholas, Minerva S. Buerk, and William T. Ford. Arch. Int. Med., 85: 305–358, Feb. 1950; 496–541, Mar. 1950; 699–721, Apr. 1950: and 819–886, May 1950.

A review of papers appearing in world literature since July 1, 1948. Review includes all phases of syphilis, as well as treatment, reactions, control, and education.

ARCH. OPHTH., CHICAGO

Uses of naphazoline (Privine) in ophthalmology. Paul Hurwitz and John M. Thompson. Arch. Ophth., 43: 712-717, Apr. 1950.

Included among the patients treated were two with syphilitic interstitial keratitis. Both had photophobia which was relieved with 0.1 percent of naphazoline hydrochloride solution instilled three times a day.

Indications and results in keratoplasty.
Harold G. Scheie. Society Transactions.
College of Physicians of Philadelphia.
Arch. Ophth., 43: 785-788, Apr. 1950.

Corneal transplantations performed on 22 eyes at the University of Pennsylvania included 6 patients whose central corneal scars were results of old keratitis, keratoconus, and interstitial keratitis. All the patients obtained clear grafts and improved visual acuity.

BRIT. J. SURG., BRISTOL

The surgery of the innominate artery, with special reference to aneurysm. Gordon Gordon-Taylor. Brit. J. Surg., 37: 377-404, Apr. 1950.

Of several case histories presented are two of patients who had syphilis. One, a man, had imperfect syphilis treatment and died of hemorrhage following operation. A woman died despite antisyphilitic measures and other therapy directed to the cardiovascular system.

Brit. J. Ven. Dis., London

Ophthalmia neonatorum. Arnold Sorsby. Brit. J. Ven. Dis., 26: 57-62, June 1950. Factors contributing to the decline are the Credé technic, compulsory notification and facilities for treatment, and newer methods of treatment. Both sulfonamide and penicillin therapy are discussed. The hope for elimination lies in an intensive study of various maternal infections which may lead to the infection,

Serological syphilis control in pregnancy. Olav Idsøe and T. M. Vogelsang. Brit. J. Ven. Dis., 26:63-68, June 1950.

Syphilis in Bergen, Norway, during and after World Wars I and II is discussed. Following World War II, syphilis was more prevalent among women than men.

For this reason, steps were taken to prevent congenital syphilis. During the period of 1944–48, serologic tests in pregnant women led to the discovery of 44 cases of syphilis. As a result 35 healthy infants were born.

Gonorrhea and penicillin. Is a six months' surveillance period necessary? W. F. Macfarlane. Brit. J. Ven. Dis., 26:69-72, June 1950.

Case histories of 2,600 penicillintreated gonorrhea patients were examined with a view to determining whether the observation period should exceed 3 months. Complications developing before or after penicillin administration failed to justify extension of the time. Default occurred usually within the first 3 months. A longer period was not considered necessary as a routine procedure.

CALIFORNIA MED., SAN FRANCISCO

The newer antibiotics in dermatology. Frederick G. Novy, Jr. California Med., 72:201-203, Apr. 1950.

The article is a review of the literature and gives the description and uses of polymyxin, chloramphenicol, and aureomycin. Experimental studies using aureomycin and Chloromycetin in venereal diseases are reviewed.

CANAD. PHARM. J., TORONTO

Terramycin, a new antibiotic. Elliott R. Weyer. Canad. Pharm. J., 83: 10-11. May 1, 1950.

The development, chemistry, pharmacology, clinical evaluation, administration, and dosage of the new drug are considered.

CHRON, WORLD HEALTH ORGAN., GENEVA

1949: Year of development for WHO. Chron. World Health Organ., 4: 129-145, May 1950.

One of the chief efforts of the disease control program was that of venereal disease. WHO turned toward control of treponematoses in general, rather than syphilis alone. Yaws and bejel control was undertaken in regions where prevalent. In Europe attention was focused on penicillin treatment schemes.

HOSPITALS, CHICAGO

Multiple screening for a variety of diseases.

A. L. Chapman. Hospitals, 24:37-40,
May 1950.

Article describes the multiple-screening program as used in San Jose, Richmond, and other cities. Multiple-screening tests should be specific, relatively inexpensive, and should not take more than 3 minutes to perform. Screening procedures are meant to channel people with early, undiagnosed chronic diseases to their physicians. The advantages of hospital adoption of screening procedures are discussed.

Multiple screening pilot studies. Michael Lesparre. Hospitals, 24:41, May 1950.

This is a description of the screening program at the Boston Health Protection Clinic. Patients are screened for heart disease, hypertension, diabetes, tuberculosis, cancer, syphilis, nephritis, vision and hearing defects, arthritis, and nutritional status. About 120 persons are seen each week.

INTERNAT. DIGEST OF HEALTH LEGISLA-TION, (WHO), GENEVA

Ireland. Regulations: Infectious diseases, Internat. Digest of Health Legislation, (WHO), 1: 433-455, 1950.

Chapter 2, part V. of Infectious Diseases Regulations, dated 24 March 1938, is concerned with venereal diseases. Medical practitioners are required to transmit a written notification of each person with venereal disease to the chief medical officer of the district. Names and addresses of patients are not given, but reported by number in accordance with the regulations.

J. A. M. A., CHICAGO

Penicillin-silver nitrate prophylaxis against gonorrheal ophthalmia of the newborn. Preliminary report on use of penicillin and silver nitrate combined and of silver nitrate alone. Samuel G. Watts and Morris M. Gleich. J. A. M. A., 143: 635-637, June 17, 1950.

The incidence of gonorrheal ophthalmia at Harlem Hospital was reduced considerably with use of oral administration of sulfathiazole and local application of silver nitrate. After discontinuance of combined method, the incidence became comparable to previous years. Between June 1948 and June 1949, a total of 4,565 infants received combined penicillin-silver nitrate prophylaxis with not a single proved case of gonococcic conjunctivitis being observed.

Aureomycin in the treatment of gonorrhea. Study of one hundred cases. Calvin H. Chen, Robert B. Dienst, and Robert B. Greenblatt. J. A. M. A., 143: 724-726, June 24, 1950.

In this study done at the University of Georgia School of Medicine, 50 gonor-rhea patients were given 1 gm. of aureomycin orally 3 times daily for 2 days, while another 50 were given the same dose for 1 day. Results were identical in both groups with one failure each. Toxic reactions were few and not serious.

J. KANSAS M. Soc., TOPEKA

Penicillin treatment of cardiovascular syphilis. Lloyd H. Coale, Max S. Allen, and Mahlon H. Delp. J. Kansas M. Soc., 51: 102–109, Mar. 1950.

The general problem of cardiovascular syphilis and its treatment is reviewed. Report is made of penicillin treatment of 70 patients, 47 previously treated with metals, and 23 with no previous treatment. Preliminary follow-up is submitted covering 36 of the first group and 17 of the second group. Response was essentially the same in both. The optimal amount of treatment has not been determined.

J. M. A. GEORGIA, ATLANTA

Ambulatory treatment of syphilis with aureomycin. C. H. Chen, R. B. Dienst, and R. B. Greenblatt. J. M. A. Georgia, 39: 237–238, June 1950.

Two patients with primary chancre were successfully treated at the University of Georgia School of Medicine with 1 gm. doses, four times daily at 4-hour intervals, for 2 weeks. The purpose of the study was to see if the night doses could be omitted, thus making this method more suitable for ambulatory treatment.

J. MICHIGAN M. Soc., LANSING

Ophthalmia neonatorum. W. L. Benedict. J. Michigan M. Soc., 49:560-565, May 1950.

A review is given of prophylactic measures taken to prevent ophthalmia neonatorum from the time of Credé in 1881 to the present time. Penicillin has been found to be the most effective drug of all antibiotics in the treatment; however, no suitable substitute for silver nitrate as a prophylactic agent has been found.

Michigan's Department of Health. Albert E. Heustis. J. Michigan M. Soc., 49: 590, 592, 594, May 1950.

Venereal disease in Michigan is declining. The 1949 total of 8,740 cases of syphilis was the smallest number since 1937. Incidence of congenital syphilis showed a decrease for the first time in 10 years. New gonorrhea cases have declined about one-fourth since the peak year, 1946.

J. OKLAHOMA M. A., OKLAHOMA CITY

The management of syphilis in pregnancy. David V. Hudson. J. Oklahoma M. A., 43:153-155, Apr. 1950.

A review of the literature is presented along with an account of the maternal health program of the Tulsa County Public Health Association. At the Tulsa Cooperative Clinic, no child was born with syphilis during 1947 or 1948 whose mother followed through with treatment. During this period, 67 mothers were observed through 75 pregnancies.

J. Philippine M. A., Manila

Penicillin-oil-beeswax combined with Mapharsen and bismuth in the treatment of early syphilis: An evaluation study. Antonio A. Lozano. J. Philippine M. A., 26:75-80, Feb. 1950.

Of 128 patients treated at the Manila Rapid Treatment Center, all were Filipinos except eight white patients. Treatment consisted of 300,000 units penicillin every 24 hours for 10 days, Mapharsen (0.04 gm.) intravenously every other day, and bismuth subsalicylate in oil (1.5 cc.) on the second, sixth, and tenth

days. Half of the patients lapsed from observation after treatment, while the others were observed from 1 month to 2 years. The cumulative failure rate at the end of 1 year was 6.9 percent, and at the end of 2 years was 32.1 percent.

J. ROY. INST. PUB. HEALTH & HYG., LONDON

Venereal disease in Haiti. J. Roy. Inst. Pub. Health & Hyg., 13: 186, June 1950. To eradicate venereal disease in Haiti campaign was started by WHO. Haitian

a campaign was started by WHO, Haitian Government, and UNICEF. It is estimated that one-fourth of the population suffer from syphilis or gonorrhea, while 85 percent are afflicted with yaws. About 20,000 people will be inoculated a day by 10 teams who will operate from jeeps.

The health of the Nation. Venereal diseases. J. Roy. Inst. Pub. Health & Hyg., 13: 206, June 1950.

The sharp fall in clinic figures for early syphilis noted in 1947 was repeated in 1948. The fall is less marked in large seaports. Since the number of males reporting to the clinics was so much higher than females, it is thought that many women do not realize that they are infected. The need for more education is emphasized.

LANCET, LONDON

Penicillin in the treatment of uncomplicated gonorrhoea. A. J. King, F. R. Curtis, and C. S. Nicol. Lancet, 1:701-703, Apr. 15, 1950.

Results of treatment are given for 1,788 males and 481 females. All were treated with 150,000 units of sodium penicillin in water. Follow-up was restricted to 1,447 males and 432 females. Of these, 6.4 percent of males and 3.5 percent of females were regarded as immediate failures since gonococcus persisted in secretions. Of the remaining men, 19.1 percent developed acute purulent urethritis after apparent cure, while 18.6 percent showed evidence of residual infection in the genital tract. Of the remaining women, 13.4 percent showed gonococcus in genital secretions 2 weeks or more after treatment.

Penicillin for gonorrhoea. Lancet, 1:719, Apr. 15, 1950.

The effectiveness of penicillin has filled patients and doctors with a confidence which no remedy has ever justified. The time has come for reassessment, and the plea for care and conservatism should not be ignored. Formerly gonorrhea suffered from neglect, and it would be unfortunate if harm were done through overconfidence now.

Aureomycin in lymphogranuloma inguinale. C. D. Alergant. Lancet, 1:950-951, May 20, 1950.

Of six patients with lymphogranuloma venereum treated with aureomycin, four showed good clinical response. All were kept under observation for 6 to 14 weeks. None became Frei-negative.

M. Ann. District of Columbia, Washington

The treatment of gonococcal arthritis with streptomycin. Harold L. Hirsh and Walter Kurland. M. Ann. District of Columbia, 19: 307–309, June 1950.

Case histories are presented of three patients with an initial early attack of gonococcic arthritis successfully treated with 0.5 gm. every 4 hours for periods of 6 to 10 days.

M. TECHNICIANS BULL., WASHINGTON

Cardiolipin antigen holder. Ted A. Griset. M. Technicians Bull., 1: 19–20, May-June 1950.

Special Regulation 40–305–5, Air Force Regulation 160–4, dated December 22, 1948, authorized medical installations of the Army and Air Force with the necessary equipment and properly trained technicians to use cardiolipin antigen for the serologic diagnosis of syphilis. A holder is shown for holding the antigen emulsion tube without dulling the point of the needle.

M. Times, New York.

Office gynecology. Warren A. Lapp. M. Times, 78: 272-275, June 1950.

The author discusses various complaints, among which are trichomonas vaginitis, gonorrhea, and condylomata acuminata. These can be diagnosed and treated by the gynecologist. Recommended treatment for each is given.

M. WORLD, LONDON

Unsolved problems of venereology. R. R. Willcox. M. World, 72: 231-235, Apr. 21, 1950.

The problems discussed include increased venereal disease as a result of easier treatments and more promiscuity, necessity of clinical research to bring about standardization of treatment, culture of virulent *Treponema pallidum*, unsolved problems of tissue immunity, the relationship of other treponematoses to syphilis, diagnosis of gonorrhea in women, and prophylaxis of venereal disease.

MEMPHIS M. J., MEMPHIS

Penicillin treatment of cardiovascular syphilis. Alva B. Weir, Jr., Richard H. Roberts, and I. Frank Tullis. Memphis M. J., 25: 73-77, May 1950.

Penicillin without preceding administration of heavy metals was used in treating 43 patients. During treatment attention was paid to occurrence and degree of Jarisch-Herxheimer reactions, which were noted in 8 patients. No reaction was severe enough to interrupt therapy. Evidence indicates that penicillin alone may be administered in large doses without jeopardy to patients.

NORTH CAROLINA M. J., WINSTON-SALEM

The precancerous dermatoses. S. F. Horne. North Carolina M. J., 11: 269-280, June 1950.

Of cutaneous diseases, syphilis is one considered as precancerous since it produces changes in the skin which favor development of carcinomas. Changes are in nature of ulcerated gummas and scars of late syphilitic lesions. When a carcinoma has arisen in a syphilitic lesion, the therapeutic regimen should be governed by both diseases. The syphilitic lesions will respond to penicillin, but no antisyphilitic treatment has any beneficial effect on the carcinoma.

PSYCHIATRIC QUART., UTICA

The Rorschach test and the question of "prognosis" and "recovery" in syphilitic meningo-encephalitis. G. M. Davidson and Ruth C. Conkey. Psychiatric Quart., 24:243-258, Apr. 1950.

Data are based on 20 male paretic patients at the Manhattan State Hospital in New York. In addition to regular clinical investigations, the Rorschach test was given to 10 patients before and after malaria treatment, and in the other 10 before treatment only. One-year follow-up results showed the test to be a valuable contribution toward ability to measure progress in the course of the disease. The prognostic value is greater than the diagnostic.

Pub. Health Rep., Washington

Medical examination and vaccination of farm laborers recruited from Mexico. Ralph Gregg. Pub. Health Rep., 65: 807-809, June 23, 1950.

One condition excluding laborers is venereal disease. For the fiscal year ending June 1949, 134 were excluded for this cause. The total number examined was 99,033.

RHODE ISLAND M. J., PROVIDENCE

Cardiovascular syphilis. Report from the cardiovascular division of the syphilis clinic, Rhode Island Hospital Outpatient Department. Clifton B. Leach. Rhode Island M. J., 33: 186-188, Apr. 1950.

Treatment by penicillin or bismuth with arsenicals is discussed. Advantages of maintaining a separate division for cardiovascular patients in a clinic are listed. Opinion is expressed that penicillin therapy for late syphilis need not be preceded by other preparatory medication.

Sc. News Lett., Washington

New venereal disease? Sc. News Lett., 57:355, June 10, 1950.

Former infections called nonspecific may be a new venereal disease called PPLO because it is caused by pleuropneumonia-like organisms. PPLO, discovered in 1937, can be cured with streptomycin.

SOUTH AFRICAN M. J., CAPE TOWN

Bantu syphilis. A report on 184 cases. S. V. Humphries. South African M. J., 24: 428-429, June 3, 1950.

The results of treatment of 184 Bantu are given. Various combinations of Acetylarsan, Bisantol, Mapharside, and penicillin were used. Best results were obtained in series treated with Mapharside. Of the 184, 120 obtained negative Wassermann results. The amounts of penicillin given were too small to obtain good results.

U. S. ARMED FORCES M. J., WASHINGTON

Bony lesions occurring during the early stages of syphilis. Report of a case. John H. Cox. U. S. Armed Forces M. J., 1: 788-796, July 1950.

A case of destructive syphilitic osteomyelitis of the skull occurring during the early stages of the disease is reported in a 21-year-old white man. Healing occurred approximately 8 months following therapy of penicillin, Mapharsen, bismuth subsalicylate in oil, and potassium iodide.

VIRGINIA M. MONTHLY, RICHMOND

Use of penicillin for treatment of early cases of syphilis in the city of Richmond. Paul W. Bowden and E. M. Holmes, Jr. Virginia M. Monthly, 77: 285-289, June 1950.

Of 454 patients treated at the venereal disease clinic, using 600,000 units penicillin oil-beeswax daily for 6 days, only 47 patients had a relapse and were retreated, giving an accumulated re-treatment rate of 10 percent. It is believed that penicillin therapy with either beeswax and oil or 2 percent aluminum monostearate has rendered the treatment of syphilis a duty of the private physician rather than the clinic.

Health legislation. 1950. L. J. Roper. Virginia M. Monthly, 77: 387-389, Aug. 1950.

Virginia law requires blood test be made of each pregnant woman to determine whether or not she has syphilis. Syphilis is cause of death in 80 percent of children born of infected mothers. Reports of all positive tests are filed with the Bureau of Venereal Disease Control.

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, January–March 1950

[Known military cases excluded]

norrhea	Ratio to prior quarter	All vate phy- sician sources	0.94 1.05 1.05 1.05 1.05 1.05 1.05 1.04 1.05 1.04 1.05 1.04 1.05 1.04 1.05 1.		. 94 . 86 . 38 1.01 . 88 1.00 . 90 . 90 . 98 1.03	. 90 . 92 . 90 . 95 . 90 . 90	. 95 . 97 . 99 . 83 . 75 . 82 . 76 . 1.06
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rly later	Rati prior q	All	0.96	. 99 . 987 . 90 . 92 1. 20 1. 05	1. 03 1. 16 1. 17 1. 17 1. 06 1. 42	. 85 . 85 . 96 . 96	. 98 . 97 1. 04 1. 08 (*)
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Source: PHS Form 8958-B FSA-PHS—Division of Venereal Disease, Office of Statisties 7/27/50 (ML-AS)mw.



The JOURNAL of VENEREAL DISEASE INFORMATION

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PUBLIC HEALTH SERVICE

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Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced, with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

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The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 15 cents. Subscription Price: Domestic \$1.25 a year; foreign \$1.50

Results of Penicillin Treatment in Congenital Syphilis¹

Leland J. Hanchett, M. D.,2 and Maude E. Perry 3

Most of the reports in recent literature on the subject of congenital syphilis deal with the clinical and serologic results of penicillin treatment of infants (1, 2, 3, 4). Little has been reported on follow-up observations after treatment with penicillin of the older cases, including young children and adolescents, who, from the standpoint of duration of disease, compare roughly with those patients with acquired syphilis who are properly diagnosed as having early latent or late latent syphilis.

This paper refers to patients who may present various types of stigmata but who present no signs of active syphilis and who must be diagnosed as having latent or asymptomatic congenital syphilis. In this report we propose to present clinical and serologic posttreatment observations of a group of previously untreated patients with congenital syphilis, of all age groups, who were treated with penicillin alone. The purpose is twofold: (1) to add to already published data concerning the results of penicillin treatment of early congenital syphilis (1, 2, 3, 4); (2)to bring to light from the clinical and follow-up records of these patients certain information that may serve to reemphasize already known but too often forgotten facts concerning the relationship of the duration of the disease to the results of therapy and concerning the public health implications thereof.

At the Medical Center at St. Louis between March 15, 1944, and March 14, 1948, 142 cases of previously untreated congenital syphilis were treated with penicillin alone. The inclusion in this study

of only those patients who were previously untreated and only those who were given no treatment other than penicillin makes the group a selected one from the standpoint of late complications. At this Center almost all of the congenital syphilis patients with late complications such as interstitial keratitis and late neurosyphilis were treated during this period with a combination of penicillin and fever therapy. A large number of older patients were excluded because of previous arsenobismuth therapy.

The ages of the patients in this study at the start of treatment ranged from 1 month and 4 days to 31 years and 7 months. Sixty-eight (48 percent) were under 2 years of age, 16 (11 percent) were between 2 and 4 years of age, and 58 (41 percent) were over 4 years of age (table 1). Fifty-seven (40 percent) were white and 85 (60 percent) were colored; 58 (41 percent) were male and 84 (59 percent) were female. Over half (52 percent) were first brought to treatment after they had passed their second birthday.

Table 1.—Age distribution of 142 preriously untreated patients who had congenital syphilis

Age of patient	Number of patients	Per- cent
0 to 5 months	38	26, 8
6 to 11 months	15	10.6
12 to 17 months	8	5. 6
18 to 23 months	7	4. 9
Total 0 to 23 months	68	47. 9
24 to 29 months	5	3. 5
30 to 35 months	2	1.4
36 to 41 months	3	2. 1
42 to 47 months	6	4.3
Total 24 to 47 months	16	11.3
4 to 10 years	24	16, 9
11 to 17 years	28	19. 7
18 to 24 years	5	3. 5
25 to 31 years	1	. 7
Total 4 to 31 years	58	40.8
Total	142	100.0

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³ Health Program Specialist, U. S. Public

Clinical Status of Patients

The diagnosis of congenital syphilis was made on the basis of objective clinical findings, in addition to positive serologic tests or, in some cases, positive serologic tests alone with a definite history of syphilis in the mother at the time the patient was born. In the group of 68 patients under 2 years of age, 44 (65 percent) presented one or more clinical signs of the disease (table 2). Twentyfour (35 percent) presented no demonstrable clinical signs except repeatedly positive serologic tests. Of the 44 patients under 2 years of age with one or more clinical signs of syphilis, skin and/ or mucous membrane lesions were present in 26 patients, snuffles in 13, bone and/or joint manifestations in 16, active interstitial keratitis in 1, and other manifestations in 7. Other manifestations included splenic or hepatic enlargement and corneal scarring.

In the group of 16 patients between the ages of 2 and 4 years, similar definite objective clinical signs of syphilis were much less frequently observed. Seventy-five percent had no clinical signs, while

in four patients (25 percent of the group) skin and/or mucosal manifestations were observed once, snuffles once, and bone and/or joint manifestations twice.

In the group of 58 patients over 4 years old, the number that showed definite clinical evidence of congenital syphilis was greater than in the group 2 to 4 years old. Fifty-two percent showed no clinical signs, while 48 percent showed symptoms or signs in the following frequency; rhagades, 2 cases; bone or joint manifestations, 10; Hutchinson's type of incisors, 17; active interstitial keratitis, 1; eighth nerve deafness, 1; and other manifestations, 4.

Of the entire group of 142 patients, 53.5 percent showed one or more clinical signs of congenital syphilis, and 46.5 percent showed no evidence except a positive blood serology.

Serologic tests before treatment included the standard Kahn test and a quantitative Kahn on all who showed a positive or doubtful reaction in the standard test. Of the 142 patients, 137 had positive tests, with titers ranging from 3 to 256 or more Kahn units. Ten percent of the patients had reagin titers

Table 2.—Clinical status of 142 patients who had previously untreated congenital syphilis

	Nt	ımber	of patie	ents	Skin		Bone and/or				0.42
Age distribution	No clini- cal signs	Per- cent	Clin- ical signs	Per- cent	and/or mucosal mani- festa- tions	Snuf- fles		Hutch- inson's teeth	Active inter- stitial keratitis	Deaf- ness	Other mani- festa- tions
0 to 5 months 6 to 11 months 12 to 17 months 18 to 23 months	9 8 3 4	23. 7 53. 3 37. 5 57. 1	29 7 5 3	76. 3 46. 7 62. 5 42. 9	19 3 4	8 3 2	11 2 1 2		1		6 1
Total 0 to 23 months	24	35. 3	44	64. 7	26	13	16		1		7
24 to 29 months 30 to 35 months 36 to 41 months 42 to 47 months	4 1 1 6	80. 0 50. 0 33. 3 100. 0	1 1 2	20. 0 50. 0 66. 7	1	1	2				
Total 24 to 47 months	12	75. 0	4	25. 0	1	1	2				
4 to 10 years 11 to 17 years 18 to 24 years 25 to 31 years	12 16 1 1	50. 0 57. 1 20. 0 100. 0	12 12 4	50. 0 42. 9 80. 0	1 1		4 3 3	5 10 2	1	1	1 3
Total 4 to 31 years	30	51.7	28	48.3	2		10	17	1	1	4
Total	66	46. 5	76	53. 5	29	14	28	17	2	1	11

Table 3.—Changes in spinal fluid in 95 cases of previously untreated congenital syphilis

A go distribution	Nor	mal		Total			
Age distribution	Number	Percent	Group I	Group II	Group III	Percent	10ta1
0 to 23 months 2 to 3 years 4 to 31 years	21 13 51	80. 8 92. 9 92. 7	1 2	3 1 1	1	19. 2 7. 1 7. 3	26 14 55
Total	85	89. 5	4	5	1	10. 5	95

Number includes 1 patient with doubtful spinal fluid Kolmer and no other abnormalities.

from 3 to 32 Kahn units, 34 percent from 32 to 256 Kahn units, and 56 percent over 256 Kahn units.

On two patients the quantitative test was not carried out, but both were strongly positive in the standard test. There were two babies under 6 months of age on whom a blood serology was not done; however, both had maculopapular lesions in which Treponema pallidum were demonstrated in darkfield prepara-One infant under 6 months of tions. age showed a negative Kahn, but in this case the diagnosis of syphilis was indicated by the presence of papulosquamous lesions, definite X-ray evidence of periostitis of the long bones, and a verified record of syphilis in the mother during the prenatal period.

At the time of treatment the spinal fluid was studied in 95 of the cases. Abnormalities were noted in only 10 patients (10.5 percent) (table 3). Two of these showed doubtful Kolmer tests with no other abnormalities in the fluid, leaving only 8 patients with spinal fluid changes warranting a diagnosis of neurosyphilis. One patient, 19 years old, had a group III fluid with definite personality changes in which a diagnosis of juvenile paresis was made. The other seven patients were asymptomatic as regards neurologic symptoms.

Treatment Methods

In our early experience with the use of penicillin in treating congenital syphilis, little or no information was available regarding optimum total dosages for infants. Platou and his coworkers (1) first

employed a total dosage of 16,000 to 32,000 units of penicillin per kilogram of body weight. Later the same group (2) recommended total dosages of at least 100,000 units per kilogram of body weight in syphilitic infants.

The first two patients in this series were given 500,000 units, amounting to approximately 50,000 units per kilogram of body weight. While the acute symptoms (skin lesions, snuffles, and malnutrition) improved remarkably, the serologic response was much less encouraging in that, after an initial drop in titer, further decrease was very slow indeed.

As we gained experience our anxiety concerning possible serious reactions decreased, and total dosages were increased to from 100,000 to 600,000 units of penicillin per kilogram of body weight. The average total dose for infants under 2 years of age was 300,000 units per kilogram of body weight; for those from 2 to 4 years of age, 150,000 units; and for those from 4 to 10 years of age, an average of 115,000 units. Patients over 11 years of age received from 2,400,000 to 8,000,000 units, as was recommended for adults with late acquired syphilis (table 4). Patients over 11 years of age with spinal fluid changes or active interstitial keratitis were given 3,400,000 to 8,000,000 The total dosages were not increased in infants under 2 years of age because of abnormalities of the spinal fluid.

Many of the infants in this series, especially those with symptoms of marasmus, snuffles, skin lesions, and bone or joint

involvement, required special dietary care, vitamin therapy, and good nursing. This was considered a most important adjunct to penicillin treatment.

The 3-hour time interval between injections was employed until October 1946, after which individual doses were administered every 2 hours. This change was made on the basis of the report of Cooke and Goldring (5), which suggested that the shorter time interval might prove of greater therapeutic efficiency. In July 1946 a change was also made in the type of penicillin used, the crystalline G being substituted for the old amorphous commercial penicillin.

In our early use of penicillin treatment for syphilis it was thought advisable, in order to prevent severe Herxheimer reactions, to give small initial doses of from 1,000 to 10,000 units at each injection to infants and children under 12 years of age. The size of the doses was doubled on successive days until they reached a level of from 15,000 to 50,000 units, depending on the age and general condition of the patient. Later this practice was found to be unjustified. The number of reactions to treatment was not de-

creased and the period of hospitalization was prolonged. Doses of from 15,000 to 50,000 units every 2 hours were then given from the beginning of treatment until the prescribed total dosage had been given.

Reactions to Treatment

During the treatment period, careful observations were made of each patient, including recording the temperature at 3-hour intervals. The reactions were febrile in character with one exception, which occurred in a patient 19 years of age with a diagnosis of juvenile paresis. He showed a very definite exacerbation of mental symptoms after treatment was started and subsequently required confinement in a State psychiatric hospital.

Nearly all other reactions occurred in patients under 2 years of age. A temperature elevation of more than 1° C. within 48 hours after the beginning of treatment was classified as a primary fever. A similar degree of elevation occurring after 48 hours was called a secondary fever. Irregular elevations of more than 1° C. occurring throughout the treatment period were termed intermittent fever.

Table 4.—Total dosages of penicillin in million units for previously untreated congenital syphilis patients

Ago diotnihutia	Number		Total amount of penicillin received										
Age distribution	of patients	0.5	1.2	1.5	1.8	2.0	2.4	2.8	3.4	3.6	4.0	4.8	8.0
0 to 5 months 6 to 11 months 12 to 17 months 18 to 23 months	38 15 8 7	2	1 11 3	5 1 2 1 1	9 6 14 3		10 3 2	1 1	1				
Total 0 to 23 months	68	2	17	9	22		15	2	1				
24 to 29 months 30 to 35 months 36 to 41 months 42 to 47 months	5 2 3 6		1 1 	1	1 2 1	 	2	1				11	
Total 24 to 47 months	16		3	2	4	1	3	2				1	
4 to 10 years 11 to 17 years 18 to 24 years 25 to 31 years	24 28 5 1			1	2		9 3 1		3 1 10	1 3	1	5 7 2	1
Total 4 to 31 years	58			1	2		13		13	4	1	14	10
Total	142	2	20	12	28	1	31	4	14	4	1	15	10

¹ One had positive spinal fluid test.

Table 5.—Reactions to treatment of previously untreated congenital syphilis patients

		Number	of patients		Duimous	Cosond	Inter-		
Age distribution	No reac- tion	Percent	Reaction	Percent	Primary fever	Second- ary fever	mittent fever	Other	
0 to 5 months	13	34. 2	25	65, 8	23	1	1		
6 to 11 months	9	60.0	6	40.0	5		1		
12 to 17 months	6	75.0	2	25. 0	2				
18 to 23 months	5	71. 4	$\bar{2}$	28.6	$\overline{2}$				
Total 0 to 23 months	33	48. 5	35	51. 5	32	1	2		
24 to 29 months	5	100.0							
30 to 35 months	2	100.0							
36 to 41 months	3	100.0							
42 to 47 months	5	83. 3	1	16. 7	1				
Total 24 to 47 months	15	93. 8	1	6. 2	1				
4 to 10 years	24	100, 0							
11 to 17 years	28	100.0							
18 to 24 years	4	80.0	1	20.0				1 1	
25 to 31 years	1	100.0							
Total 4 to 31 years	57	98.3	1	1.7				1	
Total	105	73.9	37	26.1	33	1	2	1	

¹ The patient with juvenile paresis became more mentally disturbed.

In the group of 68 patients under 2 years of age, 35 (51.5 percent) showed reactions to treatment, all of which were febrile in character (table 5). Of the 35 patients, 32 had a primary fever, one of which was associated with a generalized maculopapular eruption of the skin; one had a secondary fever, occurring on the eighth day of treatment; and two had intermittent types of temperature elevation. One patient, aged 3 years and 7 months, had a primary fever. None of the patients over 4 years of age had a significant temperature elevation. In the entire group of 142 cases, 37 (26 percent) showed reactions to therapy. elevations temperature varied from 100.6° F, to 104.2° F, and usually returned to normal within 48 hours.

In only five patients, all under 6 months of age, was therapy interrupted because of reaction to treatment. Therapy was resumed in each case within 24 hours and continued regularly until completion.

Ninety-five percent of the reactions observed occurred in the patients under 2 years of age. Thirty-one (53.4 percent) of the 58 patients who received increasing doses of penicillin during the first few days of treatment had reactions. Six (60)

percent) of the 10 who received doses of equal size from the beginning of treatment experienced reactions. While the number of patients in the latter group is too small for adequate comparison, the indications are that graduated doses of penicillin do not decrease the number of treatment reactions in infants.

Posttreatment Observations

Great effort was made to obtain physical examinations and quantitative serologic tests at monthly intervals of all infants and children under 4 years of age. We requested a similar check-up of patients over 4 years of age every 6 months. As was expected, serious difficulty was experienced in obtaining adherence to this follow-up routine. Many patients lived in remote rural areas where facilities for examinations were not available and where distances made transportation to the Center for examination practically impossible. Public health nurses other field workers were nonexistent in most rural areas. In addition, the socioeconomic status of the parents offered only meager cooperation at best in any plan for regular follow-up examinations

Table 6.—Results of serologic follow-up at 24 to 30 months after treatment of 75 previously untreated congenital syphilis patients

Number of pa- tients	Number nega- tive	Percent nega- tive	Number posi- tive	Percent posi- tive	Number re-treated	Percent re-treated
20 10 2 5	20 8 1 3	100. 0 80. 0 50. 0 60. 0	2 1 2	20. 0 50. 0 40. 0		
37	32	86. 5	5	13. 5		
3 1 2 4			3 1 2 4	100. 0 100. 0 100. 0 100. 0		
10			10	100. 0		
12 15	1 1	9. 1 6. 7	9 14	81. 6 93. 3	1 2	9.3
1			1	100. 0		
28	2	7. 4	24	88. 6	2	4.0
75	34	45. 8	39	52. 5	2	1. 7
	20 10 2 5 37 3 1 2 4 10 12 15 1 28	of patients negative 20 20 20 10 8 2 1 5 3 3 37 32 32 31	of patients negative negative 20 20 100.0 10 8 80.0 2 1 50.0 5 3 60.0 37 32 86.5 3 1 2 4	of patients negative negative positive 20 20 100.0	of patients negative positive positive 20 20 100.0 ————————————————————————————————————	of patients negative positive positive Number re-treated 20 20 100.0

¹ Dropped from study when re-treated with fever and penieillin.

for these children. Some follow-up observation was obtained on 124 (87 percent) of the 142 cases in this group. Seventy-five (53 percent) were observed for more than 2 years after treatment (table 6).

Twenty (53 percent) of the patients under 6 months of age were followed for more than 2 years. All of these became clinically and serologically negative. Thirty-two (86.5 percent) of the 37 patients under 2 years of age at the time of treatment who were followed for more than 2 years showed no clinical evidence of active syphilis and had become seronegative.

Ten (62.5 percent) of the patients between the ages of 2 and 4 years remained under follow-up for over 2 years. Even though none presented evidence of active syphilis, all were still seropositive at the last examination.

In the group over 4 years of age, 28 (48 percent) were still under observation at the end of the period. Of this number, 2 (7.4 percent) became seronegative, 24 (88.6 percent) remained seropositive, and 2 (4 percent) were re-treated because of recurrence of clinical manifestations.

It is believed particularly noteworthy that of those patients whose serology decreased to definite negativity, none who remained under observation showed subsequent evidence of serologic relapse.

Figure 1 shows the cumulative percentage of patients who were re-treated and the percentages of patients both under and over 2 years of age who were seropositive or seronegative at each observation period at the time of treatment. The percentage of patients under 2 years of age who became serologically negative cannot be fairly compared to the percentage of those over 2 years who became negative, for the reason that the group over 2 includes a wide range in ages and it is known that in the older age groups the rate achieving seronegativity is less. Had the number of patients in the group 2 to 4 years of age been more nearly equal to the number in the group over 4 years old, a more reasonable comparison of results of therapy in these two groups could have been presented. It is believed, however, that these graphs illustrate how greatly the probability of obtaining negative serologic results decreases with the increasing age of the patient before treatment.

The irregularity of the graph showing the percentage of patients 2 years of age and over who were serologically negative at each observation period is caused by the loss from observation of three patients who became negative and not because of serologic relapses.

The statistical method employed in this evaluation of therapy is that recommended by the Division of Venereal Disease of the United States Public Health Service (6). It is based on the assumption that patients who lapse from observation would have become seronegative, remained seropositive, or been re-treated in the same ratio as those who remained under observation.

Due to the difficulty experienced in obtaining follow-up examination at regular intervals on many of these patients, the

time at which negativity is reached cannot be determined with any degree of accuracy. In the group under 2 years of age, it was observed that, of those who became seronegative, 51 percent had obtained negative blood serologies by the end of the first posttreatment year, 73 percent by the end of the second year, 88 percent by the end of $2\frac{1}{2}$ years, and, of the remainder, one as late as 4 years and 3 months after treatment.

In the group of 16 patients between 2 and 4 years of age, three patients became negative and were lost from follow-up before 24 months. One of these became negative during the fifth month after treatment, one during the tenth month, and the third during the twenty-second month. The two in the group over 4 years old who became seronegative did so dur-

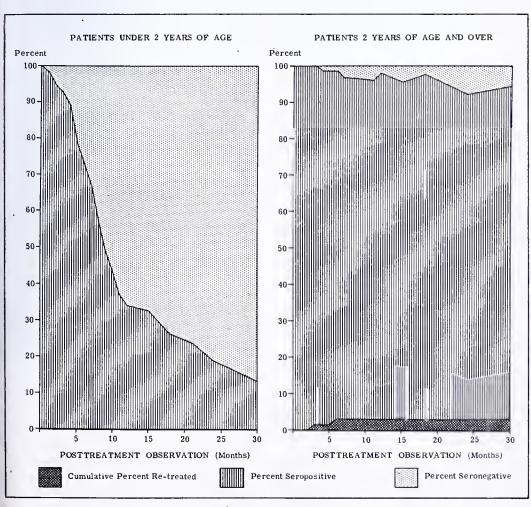


FIGURE 1.—Results of treating congenital syphilis with penicillin.

ing the fifteenth and eighteenth months, respectively.

In general it may be stated that for infants under 2 years of age there is an increased proportion of negative serologic results with each passing month after treatment. It is not at all unusual, however, for the serologic titer to decrease very slowly and first reach negativity 24 or more months after treatment. The indications are that of the children treated after 2 years of age the small percentage who may become serologically negative will have shown a still more gradual decrease in titer.

The infants who demonstrated symptoms of active syphilis improved rapidly during and immediately after treatment. There was a marked improvement in nutritional state, and skin and mucous membrane lesions cleared rapidly. The snuffles apparently cleared more slowly than the skin lesions. Serial roentgenographic studies, when obtained, showed definite improvement within 3 to 4 months in those infants who had definite bone or joint involvement.

Only two patients required re-treatment because of a recurrence of clinical symptoms. Both of these developed recurrences of acute interstitial keratitis after treatment. The first, 10 years and 2 months old, was first brought to treatment 3 months after a mild episode of interstitial keratitis of the right eye. Five months after receiving 3,400,000 units of penicillin, acute interstitial keratitis of the left eye occurred. A month after re-treatment with 8,000,000 units of penicillin, examination by the consulting ophthalmologist showed a normal appearance of the right eye and a marked improvement of the left eye.

The other patient, 10 years and 7 months old, was given 8,000,000 units of penicillin for acute interstitial keratitis of the left eye, after which the acute symptoms subsided and there was a marked clearing of the corneal opacity. She returned 2 months later with acute interstitial keratitis of the right eye. Continued clearing of the left eye had occurred during the interval. On the

second admission she received 8,000,000 units of penicillin and 33 hours of fever therapy from 104.4° F. to 106° F. Five months later she was admitted the third time with the right eye showing marked clearing but with the left eye again showing active signs. Six months after this treatment, which consisted of 19,400,000 units of penicillin with 30 hours of mechanofever from 104° F. to 105.4° F., both eyes appeared entirely quiescent.

In the group of 75 patients who were followed for over 2 years, 3 deaths were reported. Two of these, who were less than 6 months of age at the time of treatment, died at 6 and 7 months, respectively, after treatment. The cause of death in both cases was reported as pneumonia. The third death resulted from an automobile accident that occurred 2 years and 7 months after treatment. No clinical or serologic follow-up observations had been obtained in this In both of the infants who died following treatment, the serologic tests had declined to 4 Kahn units or less at the time of the last observation. In none of these three cases was there any indication that either syphilis or the treatment was a contributing factor in the death of the patient.

Five of the eight patients who had definite spinal fluid abnormalities at the time of treatment had repeat lumbar punctures from 6 months to 2 years after treatment. In two of these the abnormalities in the spinal fluid had completely disappeared, and the other three showed improvement but maintained a positive spinal fluid Kolmer.

Examination of the status of the patients who remained serologically positive throughout the observation period may reveal further information of interest. Of the 5 patients under 2 years of age at treatment who remained seropositive, all had a quantitative titer of 4 units or less on the last examination. Of the 10 children between 2 and 4 years of age, 7 (70 percent) were reported as 4 units or less, while 3 (30 percent) showed a titer of 16 units or more. In the group of 24 patients over 4 years of

age, 8 (33.3 percent) had quantitative titers of 4 units or less, while 16 (66.7 percent) were reported positive, with titers ranging from 8 to 128 units on their last examination. None of the entire group of 39 showed clinical evidence of active syphilis on the last examination.

While the definition and significance of seroresistance in latent congenital syphilis is open to much conjecture, it is believed for reasons of conservatism that all 39 of these cases may correctly be called seroresistant and considered as serologic failures. The problem of determining the relationship, if any, of seroresistance to the occurrence of late manifestations of congenital syphilis and of determining the effectiveness of penicillin in preventing them will be answered only after many more years of careful follow-up observations on greater numbers of patients.

Summary

A report is made of the follow-up observations on 75 (53 percent) of a total of 142 previously untreated patients who had congenital syphilis treated with penicillin and followed for a period of more than 24 months after treatment.

Of the 142 patients, who ranged in age from less than 6 months to 31 years of age, 52 percent were first brought to treatment after reaching 2 years of age.

Clinical manifestations of active syphilis were demonstrated in 65 percent of those under 2 years of age, in 25 percent of those between 2 and 4 years of age, while 48 percent of those 4 years of age or older showed evidence of active syphilis or of some developmental characteristic of congenital syphilis. The Kahn test was reported positive in 98 percent of the patients, with titers ranging from 3 to 256 units or more.

Treatment consisted of a single course of penicillin given over a period of 5 to 32 days in graduated or equal doses administered intramuscularly every 2 or 3 hours. The total dosage of penicillin per kilogram of body weight averaged 300,000 units for patients under 2 years

of age, 150,000 units for those between 2 and 4 years of age, and 115,000 units for those 4 years of age and over.

Patients given equal-sized doses from the beginning of treatment showed only a slightly higher percentage of reactions than those who were given graduated doses.

Ninety-five percent of the reactions to treatment occurred in those under 2 years of age. These reactions were febrile in character, ranging from 100.6° F. to 104.2° F., were of short duration, and in no case prevented completion of treatment.

There were three deaths in the group followed for the entire 24–30 month period, in none of which either syphilis or the treatment was believed to be a contributing factor.

Of those patients observed for more than 2 years, 100 percent of the group under 6 months of age at the time of treatment became clinically and serologically negative by 30 months after treatment. Of the 37 patients under 2 years of age, 86.5 percent became serologically negative and free of clinical signs of active syphilis. Of the 38 cases over 2 years of age at the time of treatment who were followed for over 2 years, 91.5 percent remained scropositive, only 5.4 percent became seronegative, and 2 (3.1) percent), both over 10 years of age, required re-treatment because of recurrence of a late manifestation of the disease.

None of the patients under 4 years of age showed signs of clinical or serologic relapse.

Conclusions

- 1. The report here presented provides additional evidence supporting the impression of others (1, 2, 3, 4) that penicilin treatment is effective in treating congenital syphilis, both in regard to therapeutic results and safety.
- 2. Further knowledge of the effectiveness of penicillin in preventing the late manifestations of congenital syphilis must wait for years of careful follow-up examinations of treated cases.

- 3. Total dosages of 300,000 units or more per kilogram of body weight may be given to infants and children with little danger of serious reaction.
- 4. In children over 2 years of age, on the basis of 30 months' follow-up, the decrease in the serologic titer to negative is the exception rather than the rule.
- 5. The high prevalence of clinical signs, as well as serologic evidence in congenital cases under 2 years of age, should facilitate more effective case finding in this age group.
- 6. If negative serologic status is to be achieved from penicillin treatment, therapy should be given, at the latest, before the age of 2 years and preferably during the first 6 months of life.

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Special Contact Investigation of the Patients of Private Physicians¹

Benson H. Sklar, B. A., M. Sc. P. H.; 2 and Leonard M. Schuman, M. D., M. Sc. 3

When patients who have early infectious venereal disease go to private physicians, their contacts constitute a reservoir of early case finding that frequently remains untapped. The relative size of this reservoir and its importance may be gaged from the fact that in down-State

Illinois private physicians report more cases of early infectious syphilis and gonorrhea than do the health department clinics. Though the venereal disease morbidity report form provides a space for the names and addresses of contacts, this information is rarely filled in, since the time required for the application of special interviewing technics precludes such interviewing of the patients by most practitioners. The lack of this information on the morbidity report form per-

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mits little or no direct action by the health department in following up the contacts of these patients.

To overcome this problem, a special method of contact investigation was developed by the Illinois State Department of Public Health in 1938. This method requires that the health department workers obtain permission from the private physicians to interview their infectious or potentially infectious patients for contact information.

No reasonable basis for evaluating this technic existed, however, until the assignment and report form (multiple epidemiologic form) was introduced in January 1944.⁴ The new form made it possible to tabulate and analyze the several types of contact investigation. This paper represents an evaluation of the results obtained by the Illinois State Department of Public Health from 1944 through 1949 in interviewing the patients of private physicians and in tracing their contacts.

Method

When a morbidity report from a private physician located in an area under the jurisdiction of a district health department is received in the Division of Venereal Disease Control, the case is assigned to an investigator, who is given any contact information on the report. If there is no contact information and the patient has primary, secondary, or early latent syphilis or gonorrhea, the case becomes a special assignment.

In these special assignments, the investigator must obtain permission from the reporting physician to interview the patient for contacts. If this permission is granted, the investigator interviews the patient and attempts to obtain the contact information that enables him to complete the investigation.

The approach to the private physician varies. Not only do different areas use different kinds of approach, but also there

are variations of technic among workers within the same jurisdiction. The individual case may determine the character of the approach. In general, our experience shows that the greatest success is obtained when service by the health department to the private physician is made the basis of the approach. The availability of drugs for treatment, the follow-up of lapsed cases and their return to treatment, the availability of rapid treatment facilities, and the availability of consultation in diagnosis, evaluation, and therapy are services that present an entree to securing the consent of private physicians to interview their patients.

Results

Physician Cooperation

As shown in table 1, during the 6-year period from 1944 through 1949, 6,588 cases reported by private physicians were assigned for special investigation from the morbidity reports of patients with primary, secondary, or early latent syphilis or with gonorrhea. The private physicians permitted 5,914 (89.8 percent) of these patients to be interviewed. The high percentage of patients whose physician gave this permission is apparent for each year.

Contacts Examined

The 5,914 patients interviewed for contacts named 5,368 contacts, of which 2,462 were examined, representing 41.6 contacts examined per 100 patients interviewed (table 2). The proportion of contacts examined to patients interviewed increased each year; whereas in 1944 only 29.8 contacts were examined per 100 patients interviewed, 61.0 were examined in 1949.

Contacts Found Infected

Table 3 reveals that in the 6-year period 23.7 contacts were found to be infected for each 100 patients interviewed. There were 1.404 infected contacts, an average of 234 cases per year, that otherwise might not have been dis-

⁴ Sklar, B. H.; Schuman, L. M.: Stimulating venereal disease morbidity reporting by private physicians. I. Follow-up of positive serologic test reports. J. Ven. Dis. Inform., 30: 160–164, June 1949.

Table 1.—Interviews permitted by private physicians in Illinois (exclusive of Chicago), 1944–49

Year	All patient tious sypt	s with earl			with prima dary syphi		Patients with gonorrhea			
	Cases reported by private	Interviews permitted		Cases reported by private	Interv		Cases reported by	Interviews permitted		
	physicians	Number	Percent	physicians	Number	Pereent	physicians	Number	Percent	
1944	1, 098 1, 332 1, 292 1, 299 842 725	952 1, 172 1, 144 1, 233 783 630	86. 7 88. 0 88. 5 94. 9 93. 0 86. 9	216 216 345 468 273 265	198 199 320 455 260 238	91. 7 92. 1 92. 8 97. 2 95. 2 89. 8	839 1,059 876 674 504 349	712 917 755 622 460 282	84. 9 86. 6 86. 2 92. 3 91. 3 80. 8	
Total	6, 588	5, 914	89.8	1, 783	1,670	93. 7	4,301	3,748	87. 1	

Table 2.—Contacts examined as a result of interviews with the patients of private physicians in Illinois (exclusive of Chicago), 1944–49

Year	All patients with early infectious syphilis or gonorrhea				Patients with primary or secondary syphilis				Patients with gonorrhea			
	of patients contacts examined per		patients ed contacts		Contacts examined		of patients	contacts	Contacts examined			
	Number of pointerviewe	Number of contract	<u> </u>	Number of pa interviewed	Number of consumptions of named	Number	Number per 100 paticnts interviewed	Number of p interviewe	Number of ecnamed	Number	Number per 100 patients interviewed	
1944	952 1, 172 1, 144 1, 233 783 630	823 1, 091 1, 071 1, 143 706 534	284 382 444 660 308 384	29. 8 32. 6 38. 8 53. 5 39. 3 61. 0	198 199 320 455 260 238	177 185 309 437 240 219	65 66 158 282 123 167	32. 8 33. 2 49. 4 62. 0 47. 3 70. 2	712 917 755 622 460 282	609 851 696 555 408 221	208 291 242 278 149 129	29. 2 31. 7 32. 1 44. 7 32. 4 45. 7
Total	5, 914	5, 368	2, 462	41.6	1,670	1, 567	861	51.6	3, 748	3,340	1, 297	34.6

Table 3.—Contacts found to be infected, 1944-49

Year	All patients with early infec- tious syphilis or gonorrhea					rimary or syphilis	Patients with gonorrhea			
	Number of	Contacts found to be infected		Number of	Contacts found to be infected		Number of	Contacts found to be infected		
	patients inter- viewed	Num- ber	Number per 100 patients in- terviewed	patients inter- viewed	Num- ber	Number per 100 patients in- terviewed	patients inter- viewed	Num- ber	Number per 100 patients in- terviewed	
1944 1945 1946 1947 1948	952 1,172 1,144 1,233 783 630	153 222 295 348 195 191	16. 1 18. 9 25. 8 28. 2 24. 9 30. 3	198 199 320 455 260 238	41 49 119 150 76 75	20. 7 24. 6 37. 2 33. 0 29. 2 31. 5	712 917 755 622 460 282	106 160 146 160 102 85	14. 9 17. 4 19. 3 25. 7 22. 2 30. 1	
Total	5, 914	1, 404	23. 7	1, 670	510	30. 5	3,748	759	20. 3	

Table 4.—Contacts found to have a venereal disease, 1944-49

	All patients with early infec- tious syphilis or gonorrhea			Patients second	with prin dary syph		Patients with gonorrhea		
Year	Contacts	Contacts found to be infected		Contacts	Contacts found to be infected		Contacts	Contacts found to be infected	
	examined	Num- ber	Percent	examined	Num- ber	Percent	examined	Num- ber	Percent
1944 1945 1946 1947 1948	284 382 444 660 308	153 222 295 348 195	53. 9 58. 1 66. 4 52. 7 63. 3	65 66 158 282 123	41 49 119 150 76	63. 1 74. 2 75. 3 53. 2 61. 8	208 291 242 278 149	106 160 146 160 102	51. 0 55. 0 60. 3 57. 6 68. 5
Total	2, 462	191	57.0	861	75 510	59. 2	$\frac{129}{1,297}$	759	58.5

covered. Each year an increasing proportion of contacts were found to be infected; whereas in 1944 only 16.1 were infected per 100 patients interviewed, 30.3 were infected in 1949. Over half (57.0 percent) of the contacts examined were found to be infected (table 4).

Contact Investigations of Patients Who Had Primary or Secondary Syphilis

A separate analysis was made of the investigations of the patients who had primary or secondary syphilis or gonorrhea, since these cases represented the bulk assigned for this special type of contact investigation.

Table 1 shows that the cooperation of private physicians in permitting these patients to be interviewed was of high caliber, since they permitted this in 93.7 percent of their 1,783 patients.

The 1,670 interviews produced 1,567 contacts, of whom 861 were examined, representing 51.6 contacts examined per 100 patients interviewed (table 2). The proportion of contacts examined per 100 patients interviewed increased each year.

Table 3 reveals that 510 of these contacts were infected, an average of 85 per year; 30.5 were found infected for each 100 patients interviewed. Again, each year an increasing proportion of contacts were found to be infected. As shown in table 4, 59.2 percent of the contacts examined were infected.

Contact Investigations of Patients Who Had Gonorrhea

The cooperation of private physicians with regard to interviewing their patients who had gonorrhea also reached a high level. Of the 4,301 special assignments, the physicians permitted 3,748 (87.1 percent) to be interviewed (table 1). These patients named 3,340 contacts, of whom 1,297 were examined; 34.6 were examined for each 100 patients interviewed (table 2). Each year an increasing proportion of contacts were examined.

Table 3 reveals that 759 of these contacts were infected, an average of 127 per year; 20.3 were found infected for each 100 patients interviewed. Each year an increasing proportion were found to be infected.

As shown in table 4, 58.5 percent of the contacts examined were found to be infected. The dccline in the actual numbers of contacts examined for gonorrhea in 1948 and 1949 is out of proportion to the smaller decline in case reporting by private physicians and reflects, for the most part, a change in policy. Whereas all contacts of gonorrhea patients were investigated prior to 1948, since that year only female contacts have been investigated.

Discussion

Six years' experience in following up the patients of private physicians, using the special method of interviewing their patients who had early syphilis or gonorrhea, indicates that this procedure is an important aspect of the venereal disease control program. It was recognized that finding the contacts of patients who have infectious syphilis or gonorrhea was of extreme importance in maintaining an effective control program. The problem of interviewing clinic patients for contacts was relatively minor. Following up the contacts of the patients of private physicians, however, was of the greatest concern, since more cases of infectious syphilis and of gonorrhea are reported by them than by any other reporting agency.

In seeking to find the contacts of the patients of private physicians, it has been found that private physician cooperation in permitting health department workers to interview their patients has been exceedingly high, especially with regard to interviewing patients who had infectious syphilis. Such cooperation can be attributed to the experience of private physicians with the activities of health department workers and with the services of these departments.

The increasing proportion of contacts examined and found infected through this special method during the 6 years indicates an increasing cooperation on the part of the private physicians and increasing effectiveness in the handling of such investigations by field personnel.

For each 100 patients that private physicians permitted to be interviewed, 41.6 contacts were examined. Of the 2,462 contacts examined, 1,404 (57.0 percent) were found to be infected. The follow-up of patients who had primary or secondary syphilis or gonorrhea yielded 510 and 759 new cases, respectively. These new cases found by reason of the special interviews for contact information would not have been discovered through the routine method of investigation.

Summary

- 1. For the past 12 years the Illinois State Department of Public Health has used a special contact investigation procedure with private physicians to obtain contact information from their patients who had early syphilis or gonorrhea. Six years ago it became possible to evaluate the procedure through the use of the multiple epidemiologic form.
- 2. Cooperation by private physicians in granting permission to interview their patients for contact information was found to be very high.
- 3. For each 100 patients interviewed, 41.6 contacts were found and examined.
- 4. An average of 234 new patients, including 85 who had primary or secondary syphilis and 127 who had gonorrhea, were found each year through using this special method.

The Development and Behavior Patterns of Immunity in Experimental Syphilis¹

R. C. Arnold, M. D.; 2 R. D. Wright, M. D.; 3 and Charlotte P. McLeod, Sc. D.4

The development of immunity in syphilis is related to the duration of the infection and the immunity mechanism of the host interacting with the disease. The effect of penicillin therapy on immunity has been studied in early and latent syphilis in the experimental animal (1, 2, 3, 4). A correlation of the results of these studies with observations in clinical syphilis may yield illuminating clues on the varying incidence figures of reinfection following the intensive and rapidly completed antisyphilitic therapies.

The behavior patterns of reinfection and immunity in acute and latent syphilis in the animal are presented in this paper.

Method

The Nichols strain of *Spirochaeta pallida* was used in all experiments. Normal rabbits were infected by an injection of 0.25 cc. of an emulsion of spirochetes into the scrotum. The challenge for susceptibility to reinfection was given in the same manner.

. Final diagnosis of the chancre was confirmed by darkfield studies. Certain groups of animals were not treated; their lesions healed spontaneously, and diagnosis of latent syphilis was made 8 months after the original infection.

The therapy in all experiments con-

sisted of 14,400 units of sodium penicillin G per kilogram of body weight, given intramuscularly in 48 doses 2 hours apart. Gland transfers were made by removing unilateral or bilateral, inguinal, and popliteal lymph nodes from the experimental animals and transplanting them animal to animal in the surgically prepared scrotal pockets of normal rabbits.

Acute Syphilis

- (a) Thirty-seven animals with infectious syphilis of 6 to 11 weeks' duration were treated with penicillin. Ten days later the animals were challenged by an injection of 0.25 cc. of spirochete emulsion in the scrotum. Twenty-seven percent of the animals developed new chancres that were confirmed by darkfield studies. The remaining animals developed asymptomatic reinfections that were confirmed by positive gland-transfer studies.
- (b) Twenty-two animals with infectious syphilis of 5 to 11 weeks' duration were treated with penicillin. The existing lesions healed; no clinical evidence of relapse was noted. Six months after the completion of therapy, the animals were challenged by the method described previously. None of the challenged rabbits developed a new chancre; 36 percent developed asymptomatic infections, and 64 percent were inmune.

These findings seem to indicate that during this 6-month posttreatment interval the biologic mechanism continued the production and enhancement of immune substances. In this study there was local chancre immunity in all animals, and reinfection occurred in only 36 percent; this is in contrast to the immunity of 73 percent and reinfection of 100 percent of the animals in study (a). If similar circumstances or conditions exist in the human, this may account for

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the relatively high incidence of reinfection during the early posttreatment period as compared to later periods.

Latent Syphilis

(c) Thirty-four animals with latent syphilis of 8 months' duration were treated with penicillin. Ten days after completion of treatment the animals were challenged by the usual inoculation. None of the animals developed an infectious lesion, this being indicative of a local tissue resistance. Fifty-three percent developed asymptomatic reinfections, and the remaining 47 percent were immune to a large inoculum of spirochetes. These two distinct responses-local immunity and complete protection against the inoculum used—led to other studies in latency to determine the duration of immunity and differences in individual response.

(d) Twenty-three animals with latent syphilis of 8 months' duration were treated; 6 months later they were challenged by the usual inoculation. The animals were observed clinically for 4 months, at which time the unilateral, inguinal, and popliteal gland transfers were made. Thirteen of the 23 recipient transfer animals that were observed for 4 months developed syphilis, indicating symptomless reinfection in 57 percent of the original animals. All the animals of the original group, except one that died, were re-treated 2 months after the lymph glands were removed, which was 6 months after the spirochete challenge. The animals were followed clinically for six more months, after which they were given second posttreatment challenge. They were observed four more months, after which lymph gland transfers were made. Five of the 16 gland-transfer animals that survived developed syphilis. This indicates that 31 percent of the original animals were susceptible to the second spirochetal inoculation, in contrast to the 57 percent observed after the first challenge and the 53 percent in study (c).

A detailed 3-year study was made of the 16 animals that survived experiment (d). During this time the latent syphilitic animals, after adequate treatment, were given two spirochetal challenges 1 year apart. The results are summarized in table 1.

Table 1.—Immunity reaction of 16 animals that survived study (d)

	Type of immunity reaction	Num- ber of animals
Both challenges.	Immune protection.	6
First challenge Second challenge	Freedom from infection. Symptomless infection due to decreasing immunity.	2
First challenge Second challenge	Symptomless infection. Freedom from infection because degree of immunity was enhanced by the second reaction.	5
Both challenges.	Symptomless infection: inadequate immunity.	3

Conclusions

In the experimental animal with early syphilis, varying types and degrees of immunity may be present during the first few months. Even though the acute infection is cured with penicillin therapy at that time, the immunity-producing mechanism continues to function so that greater protection may be noted 6 months later.

In latent syphilis, significant immunity may be demonstrated and the degree of protection may be classified in these general groups:

- 1. Immunity: Adequate protection to both challenges.
- 2. Decreased immunity: Freedom from infection following first challenge, but symptomless infection after the second.
- 3. Enhanced immunity: Symptomless infection after the first challenge, but freedom from infection following the second.
- 4. Inadequate immunity: Symptomless infection after both challenges.

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CURRENT NOTES AND REPORTS

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CURRENT LITERATURE

ACTA DERMAT.-VENEREOL., STOCKHOLM

The action of penicillin on the gonoccoccus at temperatures above 37° C. Gösta Hagerman. Acta dermat.-venereol., 30: 286-288, Nov. 3, 1950.

Effects of penicillin on a series of gonococcal strains at 36.5° C. and 39° C. are compared. Of 14 strains examined, 12 exhibited an increase in penicillin sensitivity when the incubation temperature was raised to 39° C.

AM. J. SYPH., GONOR. & VEN. DIS., ST. LOUIS

The effect of treatment on the prognosis of cardiovascular syphilis. Charles W. Barnett and Allen A. Small. Am. J. Syph., Gonor. & Ven. Dis., 34: 301-318, July 1950.

A series of 334 patients with a ortic regurgitation or saccular aneurysm treated at Stanford University Syphilis Clinic is analyzed. Symptomatic and asymptomatic cases were separated for study. Results showed that antisyphilitic therapy probably improved prognosis to some extent at any stage of cardiovascular syphilis, but was definitely more effective when given before onset of symptoms.

Studies in cardiovascular syphilis. I. A preliminary report. Paul Padget, Bruce Webster, Paul M. Densen, Claude S. Nicol, and Clayton I. Rich. Am. J. Syph., Gonor. & Ven. Dis., 34: 319-323, July 1950.

A Subcommittee on the Treatment of Cardiovascular Syphilis, authorized by the Syphilis and Cardiovascular Study Sections of the National Institutes of Health, is attempting to determine the value of penicillin in the treatment of cardiovascular syphilis. This report, based on histories of 1,020 patients at Johns Hopkins and New York Hospitals, shows that a study based on retrospective analysis of materials available in clinic files cannot provide the basis for evaluation. This first report is primarily an exercise in methodology.

Reinfection in experimental syphilis in rabbits following penicillin therapy. III. Development of immunity in early syphilis. R. C. Arnold, R. D. Wright, and Sacha Levitan. Am. J. Syph., Gonor. & Ven. Dis., 34: 324–326, July 1950.

Twenty-six rabbits with active early syphilis of 5 to 11 weeks' duration, adequately treated with penicillin, were reinoculated with a homologous strain of *Treponema pallidum* 6 months after treatment. None developed symptomatic syphilis, but 8 of 22 developed asymptomatic syphilis, as shown by lymph node transfers. Findings suggested that immunity to reinfection increased with the duration of the disease before treatment.

Reinfection in experimental syphilis in rabbits following penicillin therapy. IV. The development and character of immunity in latent syphilis. R. C. Arnold, R. D. Wright, and Charlotte McLeod. Am. J. Syph., Gonor. & Ven. Dis., 34: 327-330, July 1950.

Report presents investigative methods and results of experiments on 30 rabbits with latent syphilis of 8 months' duration, treated with penicillin, and reinoculated 6 months after treatment. None developed symptomatic syphilis; however, 13 of 23 developed asymptomatic syphilis. The immunity established persisted for periods of 6 to 28 months following adequate penicillin therapy.

Results of single and multiple injection schedules for the treatment of early syphilis with penicillin in oil and aluminum monostearate. Evan W. Thomas, Charles R. Rein, Simeon Landy, and Delmas K. Kitchen. Am. J. Syph., Gonor. & Ven. Dis., 34: 331-337, July 1950.

Of 71 patients at Bellevue Hospital given single injections of either 1,200,000 or 2,400,000 units of penicillin in oil and aluminum monostearate, 84.5 percent were seronegative when last examined. Of 67 treated with 1,200,000 units once a week for 2 weeks, 61.2 percent were seronegative, and of 68 given 4 injections, 60.3 percent were seronegative. All were followed for 6 to 20 months. Results indicate that the single-injection treatment is superior.

AM. J. SYPH., GONOR. & VEN. DIS.—CON.

Chloramphenicol (Chloromycetin) in experimental syphilis of rabbits. O. M. Gruhzit and R. A. Fisken. Am. J. Syph., Gonor. & Ven. Dis., 34: 338-341, July 1950.

In studies made in the laboratories of Parke, Davis & Co., it was found that chloramphenicol in dosages of 50 to 75 mg. per kilogram per day for 2 to 5 days did not retard or influence development of lesions in rabbits. Prolongation of treatment from 4 to 8 days in dosages of 200 mg. per kilogram per day resulted in a satisfactory curative effect with infections of 6 to 9 months' duration.

Studies of the antigenic relationship of D. granulomatis to members of the tribe Eschericheae. Henry Packer and Julius Goldberg. Am. J. Syph., Gonor. & Ven. Dis., 34: 342-350, July 1950.

Serums of rabbits immunized against the organisms were used. Reciprocal absorption studies with serums immunized against the organisms suggest that the serologic similarity between Donovania granulomatis and certain Klebsiella pneumoniae organisms is due to a haptene. Preliminary experimental human inoculations employing Klebsiella organisms failed to reproduce the lesion of granuloma inguinale.

The incidence of lymphogranuloma venereum as determined by the quantitative complement-fixation test. Norton M. Luger. Am. J. Syph., Gonor. & Ven. Dis., 34: 351-355, July 1950.

Of 451 Negro factory workers employed in Petersburg, Va., positive complement-fixation reactions were obtained in 42 percent. Among a group of 178 Negro college students and 90 white volunteers, the rate was less than 2 percent. The quantitative complement-fixation test was found to be a good method for use in public health surveys and case finding.

Gumma simulating tumor of the cauda equina. Robert G. Thompson and Robert H. Preston. Am. J. Syph., Gonor. & Ven. Dis., 34: 356-360, July 1950.

Case history is presented of a 46-yearold Negro woman who complained of pains in left leg. She was admitted to the Cincinnati General Hospital where a gumma on the spine was removed. Following penicillin therapy, the patient recovered.

Syphilide cornee in early syphilis: Report of a case. Thomas S. Saunders and George Youngstrom. Am. J. Syph., Gonor. & Ven. Dis., 34: 361-363, July 1950.

Case history is given of 30-year-old woman who was given 8.4 million units of penicillin for syphilis during fourth month of pregnancy. Six months later, lesions, believed to be late sign of early syphilis, developed on her fingers. Initial penicillin treatment failed to cure the disease in the mother but protected the infant from infection. A second course of penicillin gave a satisfactory response.

Variations of serologic pattern in patients given penicillin therapy for supposed early latent syphilis. Evan W. Thomas, Simeon Landy, and Lopo de Mello. Am. J. Syph., Gonor. & Ven. Dis., 34: 364-372, July 1950.

The difficulties in interpreting positive serologic tests are discussed. Data on 127 patients treated since 1945 at Bellevue Hospital are presented. After a follow-up period of 1 to 4 years, it was believed that all but four or five of the patients had syphilis. Thirty patients who continued to have high titers a year after treatment were re-treated. Following re-treatment, five had significant drops in titers.

Follow-up report on penicillin failures in neurosyphilis. Bernhard Dattner. Am. J. Syph., Gonor. & Ven. Dis., 34: 373-377, July 1950.

Of 388 patients treated with penicillin alone, three who exhibited spinal fluid syndromes indicating a continuous active syphilitic process were re-treated with intensified treatment. Two patients appeared to reach an inactive state following large amounts of procaine penicillin in oil with aluminum monostearate, while the third has not been followed long enough to evaluate the results.

Effectiveness of antichancroidal drugs tested by autoinoculation of bubo fluid. R. R. Willcox. Am. J. Syph., Gonor. & Ven. Dis., 34: 378–382, July 1950.

AM. J. SYPH., GONOR. & VEN. DIS.—CON.

Thirty-three patients received intradermal inoculations of 0.05 to 0.1 cc. of their own chancroidal bubb fluid and two others were inoculated with fluid obtained from their chancroidal ulcers in order to assess the value of drugs for the treatment of chancroid. Sulfonamides and streptomycin were found to have definite prophylactic action. Results are given for all drugs tested. All patients were African Negroes.

Gumma of the lung, proved by the demonstration of *Treponema pallidum*. Jay Ward Smith, Gert L. Laqueur, and Charles W. Barnett. Am. J. Syph., Gonor. & Ven. Dis., 34: 383–389, July 1950.

Case history is presented of a 38-yearold white man. Diagnosis was made on pathologic examination of the lesion after surgical removal. All serologic and spinal fluid tests were negative.

ARKANSAS HEALTH BULL., LITTLE ROCK

Strange stories in V. D. records. Arkansas Health Bull., 7: 2, 6, June 1950.

Five unusual case histories are given which illustrate how syphilis may be acquired innocently or in a strange manner, and its effect on the lives of average Americans.

Brit. M. J., London

Advisory services of the World Health Organization. Martha M. Eliot. Brit. M. J., No. 4661: 1027-1032, May 6, 1950.

In the program of venereal disease control, WHO places emphasis on early syphilis, syphilis in pregnancy, prenatal and infantile syphilis, and venereal disease infections which represent a particular problem in a certain geographical area or population group. The work that WHO has done in various countries is reviewed.

BULL. HYG., LONDON

Perspectives in venereology, 1949. R. R. Willcox. Bull. Hyg., 25: 331-343, Apr. 1950.

This is a critical review of papers pub-

lished or abstracted during the year. Gonorrhea, granuloma inguinale, non-specific urethritis, lymphogranuloma venereum, chancroid, and syphilis are reviewed from the standpoint of treatment, diagnosis, and experimentation.

CHRON. WORLD HEALTH ORGAN., GENEVA Yaws control in Indonesia. Chron. World Health Organ., 4: 193, June 1950.

Control program is being undertaken by UNICEF and WHO under the direction of Dr. K. R. Hill of the University College ef the West Indies, Jamaica. Strains from yaws and syphilis infections will be sent to the Johns Hopkins University for comparative investigations of *Treponema* strains from various parts of the world.

CIRCULATION, BALTIMORE

Penicillin treatment of patients with eardiovascular syphilis in congestive failure. Joseph Edeiken, William T. Ford, Mortimer S. Falk, and John H. Stokes. Circulation, 1: 1355-1361, June 1950.

Of 12 patients treated, no untoward reactions except for slight early febrile reactions in 2 patients were noted. Total dosage varied from 4,800,000 to 9,800,000 units, with a duration of treatment from 12 to 15 days. Case histories of two deaths are presented. It is the impression of the authors that patients with syphilitic cardiovascular disease in cardiac failure react better to the combined treatment with penicillin than those who receive only treatment for congestive failure.

HEALTH BULL, RALEIGH

Venereal disease control. Departmental report. Health Bull., 65: 12, June 1950.

Control program in North Carolina has emphasized case finding by contact interviewing and treatment of early syphilis in rapid treatment centers at Charlotte and Durham. During 1949 total admissions to the centers were 6,791. Over 7,000 satisfactory tests have been run with the filter paper microscopic serologic test developed by the Eastern Medical Center at Durham and the United States Public Health Service.

HEALTH NEWS, ALBANY

Public health approach to the heart disease problem. I. Jay Brightman. Health News, 27: 3-11, 19, July 1950.

Syphilitic heart disease is the most preventable of all types. Current public health activities directed toward prevention of syphilis and the treatment of the disease in its earliest stages avoids the later complications.

Illinois M. J., Chicago

Report of the committee on venereal disease control. Illinois M. J., 98: 61-63, July 1950.

A decrease of 14.8 percent in reported cases was noted in 1949 as compared to 1948. Total admissions in down-State Illinois rapid treatment facilities decreased in 1949 by 21 percent. Educational programs carried out in the State are described.

INTERNAT, DIGEST OF HEALTH LEGISLA-TION (WHO), GENEVA

Hungary, Decree: Control of venereal diseases. Internat. Digest of Health Legislation (WHO), 1: 543-547, 1950.

Decree regards the placing under sanitary control persons who spread venereal disease. The order for placing a person under sanitary control is issued by the local police, and one copy of the order is sent to the physician in charge of the local clinic.

Internat. Health Bull. League Red Cross Societies, Geneva

Organization and function of a mental hygiene department. A. Querido. Internat. Health Bull. League Red Cross Societies, 2: 13-18, Apr.-June 1950.

In view of expected increase of general paralysis following increase of venereal disease during and after the war, a psychiatrist and social worker were detailed to deal with the problem in Amsterdam. The psychiatrist obtains from specialists names of patients with positive tests. After the patient has received treatment, a spinal fluid examination is made twice a year. The duty of the social worker is to see that the patients keep their appointments.

The Expert Committee on Mental Health. Venereal diseases. (WHO). Internat. Health Bull. League Red Cross Societies, 2: 40-42, Apr.-June 1950.

At a meeting in Geneva in September 1949, it was recommended that consultants in psychiatry and social anthropology be attached to venereal disease control demonstration teams to study the applicability of their work to that of venereal disease control.

J. A. M. A., CHICAGO

Use of penicillin O in patients hypersensitive to penicillin G. Italo F. Volini, William H. Shlaes, and Osear Felsenfeld. J. A. M. A., 143: 794-797, July 1, 1950.

Penicillin O given by inhalation, oral troches, and parenterally was used in 57 patients sensitive to penicillin G. One patient was a 76-year-old man with syphilitic heart disease who developed urticarial rash while being treated with penicillin G. There were no reactions to penicillin O.

Conference on gonorrhea. Foreign Letters. J. A. M. A., 143: 911-912, July 8, 1950.

Conference was held at the Paris Fournier Institute in November 1949. Various types of treatments were discussed. Of 26 specialists, 23 considered 600,000 units of penicillin given in two injections sufficient therapy for women. The Congress passed a resolution that sanitary antivenereal disease education be further developed, that the liaison with armies, mercantile marines, and international authorities be regularly instructed and adapted to present necessities.

Venereal diseases in Denmark, 1900-1948. Foreign Letters. J. A. M. A., 143: 1015, July 15, 1950.

By 1918, figures were more accurate than for previous years. In 1919, there were 4,307 notifications of acquired syphilis. By 1938, this figure was reduced to 470. There was a decline in the incidence of genorrhea, with 14,507 cases reported in 1919 and only 7,803 in 1940. After return of Danish soldiers from Germany in 1944, the incidence of syphilis was nine times the incidence in 1938, and three times for genorrhea.

J. A. M. A.—CONTINUED

Reports by Drs. D. Gottlieb and Perrin H. Long at the Second Italian Congress on Antibiotics. Foreign Letters. J. A. M. A., 143: 1443, Aug. 19, 1950.

Report was presented by M. Monacelli on syphilis and antibiotics in which he stated that antisyphilitic action of penicillin is proved, but the therapeutic scheme may still be improved. He discussed absence of relation between doses employed and therapeutic effects.

J. AM. M. WOMEN'S A., NASHVILLE

WHO around the world. J. Am. M. Women's A., 5: 280-283, July 1950.

WHO has carried out surveys or given assistance to 79 countries and territories in all parts of the world. Campaigns against communicable diseases stressed malaria, tuberculosis, and venereal disease. Countries given aid and type of assistance are listed.

J. BACT., BALTIMORE

The effective concentrations of penicillin in vitro and in vivo for streptococci, pneumococci, and *Treponema pallidum*. Harry Eagle, Ralph Fleischman, and Arlyne D. Musselman. J. Bact., 59:625-643, May 1950.

Study was undertaken to determine whether the minimum effective concentration in vivo is the same, greater, or less than that necessary to kill the same organism in vitro. With $Treponema\ pallidum$ in rabbits, the minimum serum concentration that supplied a treponemicidal level at a testicular lesion was estimated to be from 0.005 to 0.01 μg per milliliter. Minimum effective serum concentrations were regularly two to five times the concentrations necessary to kill the organisms in vitro.

J. IMMUNOL., BALTIMORE

A quantitative complement fixation test: titration of luetic sera by the unit of 50 percent hemolysis. George J. Stein and Dang Van Ngu. J. Immunol., 65: 17-37, July 1950.

A quantitative complement-fixation test employing the unit of 50-percent hemolysis is described. The test proved to be highly sensitive, specific, and relatively simple to carry out. It recommends itself to careful studies in syphilitic therapy since the efficacy of antibiotics may be better established by precise determinations of antibody levels at various stages of treatment.

J. Lab. & Clin. Med., St. Louis

A rapid test for the serodiagnosis of syphilis. Six years' experience and improvements. F. Rappaport and F. Eichhorn. J. Lab. & Clin. Med., 36: 302-305, Aug. 1950.

Experiences with the Rappaport-Eichhorn test (rapid flocculation) are reported, and improvements in preparation of antigen are described. After testing 110,000 blood specimens, the authors believe the test can be relied on to combine a very high degree of sensitivity with a high degree of specificity. The test is easily and rapidly carried out thus making it suitable for mass examinations.

J. M. A. Alabama, Montgomery

Congenital syphilis. Editorial. J. M. A. Alabama, 20: 51-52, Aug. 1950.

Editorial quotes statements made by Dr. Walter Clarke, executive director of the American Social Hygiene Association, on disastrous and costly effects of syphilis and how they can be prevented by finding cases in early stages and instituting treatment. Program of American Social Hygiene Association designed to aid in fight of congenital syphilis is presented.

MINNESOTA MED., ST. PAUL

Syphilitic cardiac deaths in over fifty thousand autopsies. B. J. Clawson. Minnesota Med., 33:437-440, 479, May 1950.

Deaths due to cardiac syphilis in records of Department of Pathology, University of Minnesota, during years of 1910–47 are analyzed. Of the 422 deaths from syphilitic hearts, 58.5 percent were due to aortic insufficiency, 18.9 percent to narrowing of coronary orifices, 21.1 percent to aortic aneurysm, and 1.4 percent to gumma of the myocardium. Males predominated in the ratio of nearly 3 to 1. The greatest number per thousand autop-

MINNESOTA MED., ST. PAUL—CONTINUED sies of both sexes died in the fifth and sixth decades. No deaths occurred in the first and second.

MISSISSIPPI DOCTOR, BOONEVILLE

Present tendencies in antibiotic therapy. W. C. Thompson. Mississippi Doctor, 28: 93-96, Aug. 1950.

In discussing antibiotics, the author lists drugs of choice for various diseases. Of the venereal diseases, penicillin G is given for both gonorrhea and syphilis; aureomycin, Chloromycetin, and streptomycin for chancroid; Chloromycetin and aureomycin for both granuloma inguinale and lymphogranuloma venereum.

MOD. MED., MINNEAPOLIS

Problems in syphilis diagnosis and therapy. Mortimer S. Falk. Mod. Med., 18: 53-60, June 15, 1950.

Common problems in modern treatment are discussed. These problems include those of seroresistance; difficulty of distinguishing between seroresistance, relapse, and reinfection; significance of positive cord Wassermann; justification of diagnosis of congenital syphilis; and biologic false-positive reactions.

NEW ENGLAND J. MED., BOSTON

Report of the committee on public health. New England J. Med., 243: 108, July 20, 1950.

A request was made by the director of the Division of Venereal Diseases of Massachusetts for the State Laboratory to send the Division duplicate copies of all positive blood tests for syphilis. Copies will be kept on file for 60 days, at which time morbidity records will be checked to determine whether or not the physician has reported the patient as having syphilis. If no report has been received, a letter will then be written to physician.

Premarital-examination law. Nicholas J. Fiumara. New England J. Med., 243: 238–240, Aug. 10, 1950.

The amended premarital examination law which became effective May 21, 1950, for the State of Massachusetts is discussed as to purpose of the law and procedure after syphilis has been discovered.

Preliminary report on the health protection clinic. Claire F. Ryder and Vlado A. Getting. New England J. Med., 243: 277-280, Aug. 17, 1950.

Report is given on progress of the Health Protection Clinic in Boston since it opened in January 1950. Screening is done for heart disease, hypertension, diabetes, tuberculosis, cancer, syphilis, nephritis, vision and hearing defects, and nutritional status. Clinical procedures are described. Of over 2,000 persons examined, only two definitely proved cases of syphilis were found.

NEW YORK STATE J. MED., NEW YORK

Venereal disease in pregnancy. Theodore Rosenthal, Edwin M. Gold, Helen M. Wallace, Jere B. Faison, and George Kerchner. New York State J. Med., 50: 989-991, Apr. 15, 1950.

In an 18-month period ending July 1949, of 1,097 pregnant women given serologic tests for syphilis in the New York City clinics, 6.6 percent were found to be positive. Of 1,041 tested for gonorrhea, 1.6 percent were positive. syphilis rate was higher than that for the general population.

NORTHWEST MED., SEATTLE

blind

baby. Andrew de Northwest Med., 49: 380-382, June 1950. One cause of blindness discussed is gonorrheal ophthalmia which is now rare

due to the Credé prophylaxis. At the beginning of the century, 20 to 30 percent of the inmates of institutions were blind because of this.

OBST. & GYNEC. SURV., BALTIMORE

Obstetrical and gynecological aspects of proctology: review of literature with comments. Robert Turell. Obst. & Gynec. Surv., 5: 159-170, Apr. 1950.

Among the diseases considered in this general review of pertinent proctologic data as they relate to obstetric and gynecologic problems, the author includes condylomata acuminata, trichomonas. lymphogranuloma venereum, granuloma inguinale, and gonorrhea.

OHIO PUB. HEALTH, COLUMBUS

The concept of multiphasic screening. A. L. Chapman. Ohio Pub. Health, 14: 1-4, Apr. 1950.

Advantages are a saving in administrative expense, cost of personnel, and usefulness in control of chronic diseases. Examination of blood for syphilis, anemia, and diabetes, and chest X-ray are suitable tests for multiphasic screening.

PHILIPPINE M. WORLD, MANILA

Studies on serological tests among brides and grooms and prenatal cases in the City of Manila. Jaime O. Quiason. Philippine M. World, 5: 72–75, Mar. 1950.

Of the first 545 premarital blood tests, 17 percent were found to be Kahn positive. Of 12,000 mothers tested, 14 percent were Kahn positive. Because of shortage of laboratory facilities, compulsory blood tests cannot be instigated. These given were voluntary cases.

PUB. HEALTH NEWS, TRENTON

Licensing of public health laboratory technicians. John E. Bacon. Pub. Health News, 31: 240-243, Aug. 1950.

An act to license public health technicians was signed by the Governor of New Jersey and became effective July 1, 1950. The law defines a technician as anyone appointed by a board of health to perform bacteriologic, serologic, chemical, and related technical laboratory tests.

SCIENCE, WASHINGTON

News and notes. Science, 112: 240, Aug. 25, 1950.

A new staining technic for diagnosis of skin and tissue diseases due to fungus infections has been developed by the Department of Dermatology and Syphilology in the University of Pennsylvania School of Medicine. Test makes it possible to differentiate between suspected cases of cancer, tuberculosis, and syphilis, and the diseases traceable to fungi.

SIGHT-SAVING REV., NEW YORK

Causes and prevention of blindness in children. C. Edith Kerby. Sight-Saving Rev., 20: 67-80, Summer 1950.

Series of statistical studies by the Com-

mittee on Statistics of the Blind show ophthalmia neonatorum caused blindness in 7.5 percent and syphilis in 3.2 percent of total pupils enrolled in school year 1947–48; from 1935–36 to 1947–48 ophthalmia neonatorum decreased 39 percent and syphilis 50 percent among the causes.

Syphilis and blindness. Joseph V. Klauder and George P. Meyer. Sight-Saving Rev., 20: 99-105, Summer 1950.

The outstanding causes of blindness of syphilitic origin are primary atrophy of the optic nerve of acquired and of congenital syphilis and interstitial keratitis of congenital syphilis. Authors appeal to ophthalmologists and to the component divisions of the Committee on Statistics of the Blind for more interest in syphilis as a systemic disease, in its public health aspects, its treatment, and in the early diagnosis of optic nerve involvement.

Use of statistics in planning prevention of blindness programs. Anne E. Geddes. Sight-Saving Rev., 20: 110-115, Summer 1950.

The 1940 study of Causes of Blindness Among Recipients of Aid to the Blind is discussed. Author thinks that the prevalence of blindness resulting from syphilis which, in this study, was estimated to have accounted for somewhere between 13.5 and 20 percent of the blindness among the recipients in the study sample, would decline appreciably as a result of increasing emphasis on the newer types of therapy, premarital blood tests, blood tests for women in early pregnancy, and mass serologies.

WHO and eye health. Around the World. Sight-Saving Rev., 20: 122, Summer 1950.

Under WHO and UNICEF supported programs in seven European countries against syphilis and gonorrhea, and in similar programs to be activated in 1950 for several countries in the eastern Mediterranean, southeast Asia, and the Americas, eye infections resulting from these diseases will be treated in infants and children. Stress will be put on serologic and clinical examination of pregnant mothers.

SOUTH AFRICAN M. J., CAPE TOWN

The serodiagnosis of syphilis: Its standardization. Editorial. South African M. J., 24: 596, July 22, 1950.

The need to standardize laboratory procedures for the diagnosis of syphilis is discussed. An international conference planned by WHO to take place in 1951 or 1952 will do much to achieve a uniformity in serologic tests.

STATIST. BULL. METROP. LIFE INSUR. Co., NEW YORK

Good health serves the nation. Statist. Bull. Metrop. Life Insur. Co., 31: 5-8, July 1950.

Death rates per 100,000 persons, all ages, from selected causes are given for the first 6 months of 1942 to 1950. Deaths from syphilis have declined yearly from 10.5 in 1942 to 5.4 in 1950.

STATISTICS

Mortality Due to Syphilis in the United States, 1945–48, and in Certain European Countries ^a

	All dea	aths due to s	yphilis	Deaths under 1 year due to syphilis			
Year and eountry	Number	Percent of total mortality	Rate per 100,000 population	Num- ber	Percent of syphilis mortality	Rate per 1,000 live births	
1945 FranceSweden	612, 990 71, 752	0. 3 . 1	4. 5	351 6	19. 8 12. 0	^b 0, 56	
United States	1, 401, 719	1.0	10.7	684	4.9	. 25	
1946 Italy 6 Norway Scotland Spain	539, 915 29, 220 64, 605 348, 116	.5 .4 .3 .4	6. 2 4. 2 4. 2 5. 5	753 15 12 319	26. 9 11. 8 5. 5 21. 6	0.74 .21 .11 ^d .55	
United States	1, 395, 617	. 9	9.3	538	4. 2	. 16	
Austria England & Wales & Ireland North Ireland f Netherlands Switzerland	90, 027 515, 591 44, 061 16, 913 77, 646 51, 384	. 5 . 4 . 1 . 4 . 6 . 3	6. 9 5. 5 1. 9 4. 6 4. 7 3. 9	72 83 24 5 83 11	15, 7 3, 6 42, 9 8, 1 18, 7 6, 2	0. 56 . 09 . 35 . 16 . 31 . 13	
United States	1, 445, 370	. 9	8.8	517	4.1	. 14	
Denmark 1948 France Composition Portugal United States	35, 981 506, 277 107, 576 1, 444, 337	.2 .3 .4	2. 1 4. 0 6. 0	3 274 281 438	3. 4 17. 4 60. 6	0.04 6.32 1.27	

a Countries from which recent data are available.

Provisional data.

· Civilian data only.

FSA-PHS—Division of Venereal Disease, Office of Statistics, 7/20/50 (EJD—ML—AS)gh.



^b Excludes live births dying before birth registration (3 days).

d Excludes live births dying in the first 24 hours.

[/] Civilian mortality, total population.

Source: Foreign data from Epidemiological and Vital Statistics Report, World Health Organization, October 1949. United States data from Vital Statistics Reports, NOVS, vol. 34, No. 50, June 1, 1950, and vol. 31, No. 3, May 1949.



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FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE

Submission of Manuscripts

In order to facilitate the handling of manuscripts submitted for publication in The Journal of Venereal Disease Information, the editor requests that copy be prepared in triplicate, typewritten, double-spaced. with liberal margins. Statistical tables and charts should be set up according to the style used in the Journal, and should be presented on separate sheets, rather than within text material.

FEDERAL SECURITY AGENCY

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PUBLIC HEALTH SERVICE
LEONARD A. SCHEELE, Surgeon General

Editor: THEODORE J. BAUER, Medical Director Chief, Division of Venereal Disease

The printing of this publication was approved by the Director of the Bureau of the Budget on February 26, 1948

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1950

For sale by the Superintendent of Documents, U. S. Government Printing Office Washington 25, D. C. - Price 15 cents. Subscription Price: Domestic \$1.25 cents a year; foreign \$2.00

The Treatment of Neurosyphilis: Penicillin Alone Versus Penicillin Plus Arsenic and Bismuth¹

Edgar B. Johnwick, Senior Surgeon

This presentation attempts a comparison of the results obtained with two schedules in the treatment of neurosyphilis. The purpose of the comparison is to determine whether treatment results are enhanced by the addition of arsenicals and bismuth to a schedule using penicillin.

Material

The patients admissible to the United States Public Health Service Medical Center are a selected group. They are housed in dormitories, eat in a central cafeteria, and are treated on an ambulatory basis. Therefore, no patients with severe psychoses are included in this review. Since clinical findings in the group are minimal, absent, or representative of such end results as the loss of deep reflexes, no attempt is made to introduce an appreciation of clinical improvement into the comparison of response to the two schedules. A total of 879 patients was treated with the two schedules.

Method

Upon admission, the patient's history was obtained and a physical examination performed. The laboratory tests included quantitative determinations of the serologic test for syphilis (STS) by the Kahn technic and a study of the cerebrospinal fluid (CSF) from the cisterna magna before treatment was given. results of these first examinations are recorded as admission findings in the following report. Subsequent to studies, the patients were placed on treatment schedules at random, so that equal numbers were placed on each schedule alternately. However, before the entire group of patients had been collected the administration of arsenicals was discontinued, which accounts for a greater number having been subsequently assigned to the schedule containing penicillin only. The two schedules are described as follows:

- 1. θ - θ - θ .—Penicillin in peanut oilbeeswax, administered daily in a dose of $1\frac{1}{3}$ ml. (400,000 units) for 15 consecutive days by intramuscular injection.
- 2. 8-60-5.—The same schedule as 0-60-0, plus the administration of 0.06 gm. Mapharsen in 10 ml. water intravenously on the first, third, fifth, seventh, ninth, eleventh, thirteenth, and fifteenth days, and $1\frac{1}{2}$ ml. bismuth subsalicylate in oil given intramuscularly on the first, third, fifth, tenth, and fifteenth days.

Follow-up

All patients with neurosyphilis were instructed to return to the clinic at 6-month intervals for reexamination, which included interval history, physical examination, quantitative STS, and a repeated study of the CSF. Follow-up is to continue for 4 years following the completion of treatment. To date, of the 879 patients in this study, 65.1 percent have been followed for 6 months, 37 percent for 12 months, and 22.6 percent for 18 months. The samples included in the follow-up are defined as follows:

- 1. Admission.—All patients who were admitted, treated, and seen subsequently at least one time.
- 2. 6 months.—All patients who returned to the clinic during a period of 25 to 36 weeks after admission.
- 3. 12 months.—All patients who returned to the clinic during a period of 49 to 60 weeks after admission.
- 4. 18 months.—All patients who returned to the clinic during a period of 73 to 84 weeks after admission.

¹ From the U. S. Public Health Service Medical Center, Hot Springs, Ark. With the assistance of Miss Joyce Q. White.

Measurements

The only tests with which this review is concerned are the following:

- 1. STS.—Quantitative Kahn test.
- 2. Cells.—Cell count performed on cisternal fluid within one-half hour after puncture. Cell counts are reported in whole numbers. The Fuchs-Rosenthal chamber was used during a part of the study, and such findings have been converted by division of the result by 3, using the nearest whole number in the recorded cell count. The normal cell count is considered by us to be below four cells per cubic millimeter of fluid.
- 3. Total protein.—Determined on cisternal fluid on the same day that the fluid was obtained. The Summerson sulfosalicylic acid method is used, and the resulting turbidity is compared in a Klett-Summerson photometer (1). The normal value on cisternal fluid in our experience is below 25 mg. percent.

Observations

- 1. The race-sex distribution of cases on the two schedules shows that a larger proportion of white persons is included in the 0–60–0 group (39.1 percent) as compared to the 8–60–5 schedule (34.2 percent). The proportion of females is also higher in the 0–60–0 group—43.4 percent as against 40.8 percent in the 8–60–5 group (table 1).
- 2. The age distribution of cases assigned to the two schedules shows a considerable difference, the group on the 8-60-5 schedule being younger than those on the 0-60-0 schedule. The median age of the patients on the 8-60-5 schedule falls in the 31- to 35-year age group, whereas that of the patients on the 0-60-0 schedule falls in the 41- to 45-year group. The mode, however, appears in the same age group (36 to 40 years) for both schedules. It is to be noted that 23 percent of the patients on the 8-60-5 schedule are under 25 years of age, but that only 7.6 percent of the patients on the 0-60-0 schedule are in the same young age group (table 2).

Table 1.—Distribution of patients by race and sex on first admission

Dogs and say	Number	Percent	age distr schedul	ibution by
Race and sex	of patients	0-60-0	8-60-5	Both schedules
Negro: Male Female White: Male Female Total	276 272 228 103 879	29.6 31.3 27.0 12.1 100.0	35.7 30.0 23.5 10.8	31.4 31.0 25.9 11.7

Table 2.—Distribution of cases by age on first admission

A go gnoven	Number	Percentage distribution by schedule			
Age group (years)	of patients	0-60-0	8-60-5	Both sched- ules	
16 to 20	33 74 88 112 175 125 125 65 41	2.1 5.5 8.9 10.6 20.2 15.7 16.8 8.4 5.3 6.5	7.7 15.3 12.7 17.7 19.2 10.8 8.1 5.0 3.1	3.8 8.4 10.0 12.7 19.9 14.2 2 14.2 7.4 4.7	
Total	879	100.0	100.0	100.0	

- 3. The distribution of patients by diagnosis on the first admission shows that 73.4 percent of the patients on the 8-60-5 schedule, as against 52 percent of the patients on the 0-60-0 schedule had asymptomatic neurosyphilis (table 3). It must be remembered that the clinical findings in the symptomatic cases of neurosyphilis were minimal. Only 5 cases of darkfield-positive syphilis (0.8 percent) are represented in the 619 patients on the 0-60-0 schedule, but 15 cases of darkfield-positive syphilis (5.8 percent) are included among the 260 patients on the 8-60-5 schedule.
- 4. A comparison of the average quantitative blood STS responses in the patients who were not re-treated shows that the response was similar after use of the 0-60-0 and 8-60-5 schedules (table 4).

Table 3.—Distribution of patients by diagnosis on first admission

=	Schedule				
Diagnosis	0-6	0-0	8-60-5		
	Number	Percent	Number	Percent	
Asymptomatic neurosyphilis (less than 4 years' duration) Asymptomatic neurosyphilis (more than 4 years' duration) Paresis Tabes Taboparesis Meningovascular syphilis	94 228 87 105 18 87	15. 2 36. 8 14. 0 17. 0 2. 9 14. 1	88 103 22 37 0 10	33.8 39.6 8.5 14.2 0 3.9	
Total	619	100.0	260	100.0	

5. A comparison of the average CSF cell counts in the patients who were not re-treated shows that after the use of the 0-60-0 schedule or the 8-60-5 schedule, the cell counts fell to normal and remained so for 18 months (table 5). The average initial cell count of patients in the 0-60-0 group was lower (38.3 cells) than the CSF cell count of patients in the 8-60-5 group (50.3 cells). The admission cell counts of those patients on either schedule who were eventually retreated showed a yet greater disparity. The initial CSF cell counts in 16 patients treated with the 0-60-0 schedule and later re-treated ranged from 0 to 150, the median being 20 and the average, 42. Six of these patients had over 50 cells, and three had over 100 cells. The initial CSF cell counts in 21 patients treated with the 8-60-5 schedule and later retreated ranged from 1 to 300, the median being 64 and the average, 88.1. Fifteen of these patients had over 50 cells, and 7 had over 100 cells.

6. A comparison of the average CSF total protein determinations in the patients who were not re-treated shows that after the use of the 0-60-0 or 8-60-5 schedule, the CSF total protein average remained below the maximum normal figure throughout follow-up (table 6). There were no remarkable differences among the total protein responses in patients who failed following the use of either schedule.

7. A comparison of the adjusted cumulative re-treatment rates shows that the re-treatment rate for the 8-60-5 schedule

Table 4.—Average quantitative STS titer observed during follow-up period in 835 patients who were not re-treated

Oshodula	Quantitative STS titer					
	(Kahn units)					
Sched ule	Admis-	6	12	18		
	sion	months	months	months		
0-60-0	112.1	25. 4	12. 9	12.4		
8-60-5	120.7	23. 1	9. 9	11.7		
Both schedules	114.6	24.7	12. 2	12, 4		

Table 5.—Average CSF cell counts observed during follow-up period in 835 patients who were not re-treated

-	CSF cell count					
Schedule	Admis- sion	6 months	$^{12}_{ m months}$	18 months		
0-60-0 8-60-5	38. 3 50. 3	1. 2 1. 3	0.8	0. 9 1. 4		
Both schedules	41.7	1. 2	.8	1.0		

Table 6.—Average CSF total protein observed during follow-up period in 835 patients who were not re-treated

	CSF total protein (mg. percent)					
Schedule	Admis-	6	12	18		
	sion	months	months	months		
0-60-0	32. 5	19.0	21. 7	22. 9		
8-60-5	31. 7	20.2	14. 8	18. 7		
Both schedules	32. 3	19.3	20.0	21. 8		

Table 7.—Adjusted cumulative re-treatment rate compared for the two schedules of treatment

				Sche	dule			
Observation period	0-60-0				8-60-5			
	a	b	c	d	a	b	c	d
6 months 12 months 18 months	409 231 145	5 6 5	1. 22 2. 57 3. 32	1. 22 3. 79 7. 11	163 94 54	4 12 5	2. 45 12. 45 7. 88	2. 45 14. 90 22. 78

a—Cases observed during this period.

b—Cases re-treated during this period.
c—Adjusted percent of cases re-treated during this period.

d-Cumulative percent of cases re-treated during this period.

was almost three times as high for the 18-month period as that for the 0-60-0 schedule (table 7).

8. It is difficult to analyze the findings that led to the decision to re-treat each case. Since the patients in the series did not include an appreciable number with symptoms and signs that lent themselves to effective evaluation, it follows that the signals for re-treatment were observed in the follow-up laboratory examination of the blood and spinal fluid. Those findings may be classified as improvement, resistance, or relapse. The re-treated cases are compared in table 8.

Table 8.—Comparison of chief reasons for re-treatment of patients

	Schedule			
Indication for re-treatment	0-60-0- Num- ber of failures	Num- ber of		
STS relapse onlySTS resistance onlyCSF relapseCSF resistance_Physical findings	1 1 7 5 2	4 0 7 9 1		
Total number of patients re- treated	16 619	21 260		

Discussion

Distribution of patients by race and sex.—There seems to be no significant weighting of patient selection by race or sex to either of the schedules.

Distribution of patients by age.—It appears that some selection occurred, weighting the 8-60-5 schedule with younger patients. This is supported by the fact that the greater proportion of darkfield-positive lesions (5.8 percent against 0.8 percent) was found among the patients placed on the 8-60-5 schedule, and by the fact that a greater proportion of asymptomatic neurosyphilis occurred in the same group on the first admission. It can be deduced that the patients who were placed on schedules containing penicillin plus arsenic and bismuth had been infected a shorter time than had the patients who were treated with penicillin alone. If all other factors were equal, it could then be expected that the patients on the 8-60-5 schedule would have had a better prognosis according to the conclusions reached by Hahn and Clark (2). However, as this expected favorable outcome was not observed, it appears that some other factor, more important than the age of the infection, may have influenced the outcome of treatment. illogical to deduce that the addition of arsenic to a penicillin treatment scheme made the spinal fluid response poorer, or that patients in an older age group do better after treatment for neurosyphilis if arsenic is withheld. It appears more likely that, in this series, the CSF cell count provided a better prognostic sign than did the age of the infection.

Follow-up.—In both groups of patients asymptomatic neurosyphilis was the predominant initial diagnosis (table 3), and

treatment failures were most often signaled by laboratory findings (table 8). The number of persons re-treated on the basis of physical findings was insignificantly small (table S). From this, it can be concluded that symptoms did not serve as stimuli for patient return. Of the 619 patients originally placed on the 0-60-0 schedule, 66 percent returned in 6 months; 39 percent, in 12 months; and 24 percent, in 18 months. Of the 260 patients on the 8-60-5 schedule 63 percent returned in 6 months; 36 percent, in 12 months; and 21 percent, in 18 months. Since follow-up success was almost equal for the two groups, it is considered significant that the resultant cumulative retreatment rate was considerably higher for the group treated with the 8-60-5 schedule (table 7).

STS response.—In the patients placed on the two schedules who did not require re-treatment, an identical pattern is shown in STS response. The original records of quantitative STS were expressed in Kahn units in the progression 4, 8, 16, 32, 64, 128, etc. The "average" STS expressed in table 4 is nonexistent and may be interpreted to read 64 Kahn units as the admission finding for both schedules, and 16 units, 8 units, and 8 units for 6, 12, and 18 months, respectively. The rate of achieving success is the same with either schedule.

CSF cell count.—Findings as to the CSF cell count suggest that bias entered into

on the treatment schedules. This is perhaps the expression of an urge by the physician to assign a patient with a more abnormal laboratory finding (a higher cell count) to a schedule which contains a greater amount of medication. Such selection was not supposed to occur in this study, but the evidence shows that this bias exists and that the outcome may be the result of selection rather than of the treatment schedules used.

Conclusion

It appears from the foregoing study that nothing was gained by the addition of eight injections of Mapharsen and five injections of bismuth to a schedule using penicillin for the treatment of asymptomatic neurosyphilis. It also appears likely that a bias entered into the selection of cases, from which it may also be concluded that in this series a high initial cerebrospinal fluid cell count carries more weight as a prognostic sign than does the duration of the syphilitic infection being treated.

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Suggested Technics for Mass Health Education at County Fairs

Charles R. Freeble, Jr., M. D.; Earl O. Wright; James F. Donohue; and Allen D. Pratt

In a previous issue 3 of The Journal of VENEREAL DISEASE INFORMATION WE presented a description of the venereal disease tent show that played at eight county fairs and at the State Fair in Ohio in 1948. Since then the Ohio Department of Health has had much more experience in venereal disease education at county fairs, and it occurred to us that it might be worth while to describe the technics employed in the program, including the program planning, the advance field consultation with local health departments and fair boards, the importance of tent location on the fairgrounds, and the problems encountered during actual operation of the show.

First we should like to present briefly the results of the 1949 fair program, which was presented in Ohio as part of the July and August intensive national venereal disease education campaign. Two tent-show units appeared at 19 county fairs and at the Ohio State Fair. The gate attendance at these 20 fairs was reported by the Ohio Fair Board to have been 1,153,500. It was estimated by means of sample counts that 250,685 persons (21.7 percent of the total attendance) visited our tent show and saw our films. We distributed 270,075 pieces of literature and 75,000 venereal disease book matches.

During the past two seasons we presented the exhibit at 28 fairs before more than 350,000 people, meeting many problems and solving most of them. We

should like to pass along the benefit of our experience to those who may be considering a tent show as part of their venereal disease education program. The same technics would apply to any other mass health education program, this approach not being limited in any sense to venereal disease.

Although we had two units operating on the fair circuit last season, we shall present the modus operandi of the venereal disease tent show as a one-tent operation. The method of operating two or more units simultaneously will be discussed later.

Program Planning

Although the county-fair season does not usually start until July, it is well to begin planning the program early in the year so that all preliminary work can be done and a tentative schedule set up. A useful publication for this phase of the work is the official list of county fairs, which gives locations, dates, and the name and address of the secretary of each fair. In most States this information is published by the State Department of Agriculture or the State Fair Board well in advance of the season.

A study of the official list of county fairs will show how many can be covered Since during each by a tent-show unit. week of the season several fairs are scheduled, a choice has to be made. If all other things are equal, it is usually best to select the county with the largest population, since the audience attending the tent show usually varies directly with the total attendance at the fair. However, other factors should be considered, including the anticipated cooperation of the local health department and the county-fair board, the extent of the venereal

¹Ohio Department of Health, Division of Communicable Diseases.

² Health Program Representative, U. S. Public Health Service.

³ Freeble, C. R.: Wright, E. O.; and Bogue, R. S.: "Mass Public Venereal Disease Education—Ohio Fairs." J. Ven. Dis. Inform., 30: 196–198, July 1949.

disease problem, the location of the county with respect to other counties scheduled for the show, and the drawing power of other attractions booked for the fair.

Having made a tentative selection of the fairs to be included in the tour, each local health department concerned should be notified that the venereal disease exhibit is available if the health commissioner can make arrangements with his county-fair board for a good location for a 30- by 60-foot tent—preferably near the midway within sight of the crowd but not near the merry-go-round or any other noisy attraction. If the commissioner finds that space is not available, the tentative booking schedule must be changed and the tent show offered to another health department having a fair during This procedure is rethe same week. peated until some commissioner succeeds in arranging for tent space. When the commissioner reports that he has booked space, the date is set. The schedule is thus developed for the season.

Advance Work

As soon as the schedule has been completed, a program supervisor representing the State health department should visit every participating county. He should first visit the health commissioner in order to explain the program. This is important, because health officers sometimes confuse the tent show with other touring health units requiring less space, such as X-ray trailers. Frantic last-minute efforts to get space can be avoided by clarifying the requirements in advance. The program supervisor should also request a conference between the health commissioner, the secretary of the fair, and himself in order to check on the location of the tent, to explain the nature of the exhibit, to invite the active participation of local persons in the program, to make sure that 220-volt 3-line current will be available in the area where the tent is to be erected, to plan for local publicity, and to go over other details so that when the fair opens the exhibit will be ready to receive visitors. This conference should include a trip to the spot where the tent will be erected rather than a look at the fairground blueprint. The program supervisor must satisfy himself that the commissioner and the fair officials understand the space and location requirements of the show before ending the advance field preparations.

Getting the Show Ready for the Road

The first requirement for this traveling health exhibit is, of course, a tent. recommend using a standard carnival tent, which is 30 by 60 feet. Although such a tent may be purchased or rented and become part of the show's equipment for the show personnel to set up, we strongly recommend that the problem of setting up and tearing down the tent be left with professionals. This avoids a great deal of trouble. The contract should be made with a tent rental company for "complete service," including transporting the tent and poles to the fairgrounds, erecting it before the fair opens, and tearing it down at the close of the fair. It is necessary to make careful and continual checks with the tent company regarding show schedules in order to insure smooth operation of the unit as it moves from fair to fair. Since the exhibit cannot be set up until the tent is ready, a slip on the part of the tent company may mean missing the opening-day crowd. Tent companies usually handle rental accounts on several fairs, and it has been our experience that the tent crews are likely to become confused as to schedules and locations unless they are constantly prompted by our program supervisor.

The tent should be made of dark canvas so it can be used for daytime movies. It should also be waterproof. The complete tent service costs about \$75 per fair.

In addition to the tent, a separate front display banner is needed to indicate the nature of the exhibit and the sponsors of the show and to give the "come-on" that free movies are offered. This front banner should be so designed that it is easy to set up and tear down, as well as to fold and pack for transportation. It should be self-supporting, so that it will

not have to be secured to the tent or poles. It should appeal to the eye.

Following is a list of what we consider to be the minimum equipment for the operation of a single unit:

- 1 dark rainproof tent, 30 by 60 feet.
- 1 1½-ton panel truck.
- 1 outside banner.
- 4 spotlights.
- 60 wooden folding chairs.
- 3 sound motion-picture projectors, 16mm. type, with extra fuses.
- 1 large movie screen.
- 1 film-cleaner set.
- 1 film-splicing set.
- 1 projector-cleaning brush.
- 1 heavy wooden table, 2 by 4 by 3 feet.
- 1 film case.
- 1 tool kit with hammer, saw, pliers, screwdriver, and drill.
- 1 information booth for distribution of literature.
- 1 information-booth sign.
- 2 floor-type electric fans.
- 4 copies of each film to be exhibited.
- 1 basic electric wiring system.

The wiring system must supply power for motion-picture projection, for banner spotlights, and for internal lighting. The wiring equipment will vary with the number and location of the display panels, and an electrician should be consulted after they have been designed.

In the Ohio program we lined the tent with display panels colorfully depicting the positive aspects of the venereal disease problem rather than the dire outcome of untreated syphilis. Under our direction, the cartoon-type panels were designed and painted by an imaginative commercial artist. The finished panels were 4 by 7 feet, similar to the "flats" used in theatrical scenery. The artist also created some papier-mâché figures of the parents and children in a buoyantly healthy family. These figures and panels were illuminated with soft light from shaded lamps directed downward on the panel surface so as not to interfere with the relative darkness necessary for projecting motion pictures. Although such display panels are not absolutely necessary to a tent show, we feel that they create a gay background that blends well with the popcorn-and-lemonade atmosphere of a county fair.

The principal films shown were "Know For Sure" and "Message To Women." Other approved venereal disease films were also run occasionally to keep the program from becoming automatic. The films used in the show are exposed to heavy usage, as well as to sand, dust, and sawdust particles. For this reason the prints must be properly cared for, and at best the four copies are in rather bad condition by the end of the season. three projectors are necessary because the operation requires a continuous performance. Two of the machines are constantly in use, one showing the film and the other being readied for the alternate The third projector is used as a spare and to allow a cooling-off period for the other two. Since "the show must go on," we consider the third projector essential.

The distribution of literature is an important part of the program. Various pamphlets should be offered at the information booth located just inside the entrance to the tent. We have found that a supply allowing one pamphlet per person attending the exhibit works out well. Estimating the demand for literature in this way, the supply is usually exhausted by the last evening of the fair. Book matches with a venereal disease message are popular and move fast.

The staff necessary to operate the show consists of two men. The manager is responsible for seeing that schedules are met, for contacting the health commissioner and the secretary of the fair before setting up the show, for the maintenance of equipment, and for the show's opera-He should secure passes to the fair for his truck, his staff, and any health department guests. His helper serves primarily as the projectionist and handy man. Both men must be able to operate the motion-picture projectors skillfully, and at least one must be licensed to drive the truck. We recruit college students applying for summer work with the department and find they are quite capable of running the show. They are given a

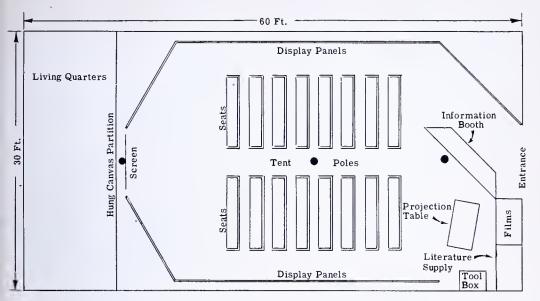


FIGURE 1.-Floor plan of Ohio VD tent show.

brief training course in venereal disease control before they start the tour so they can answer nonmedical questions intelligently. We allow them no travel money and, in the interest of economy, they live in the tent throughout the season. Cots and cooking gear provided by the department are placed in the rear of the tent behind a canvas partition. The small rear section, about 10 by 30 feet, serves as living quarters for the staff. The men not only enjoy the camp life but also guard the equipment.

A sketch of the floor plan of our tent appears in figure 1.

The Show Moves

We now have our schedule, staff, equipment, films, and literature ready, the advance work has been completed, and the show is ready to go on the road. The truck should be loaded in an orderly manner. All equipment should be securely stowed in the truck to insure against damage during travel over rough roads. The truck itself should be in good running condition and equipped with heavy-duty tires.

The truck arrives at the fairgrounds the day before the fair opens. The manager should immediately call on the secretary of the fair to learn the location of the tent. During the hustle-bustle of readying a county fair for opening day, good space is at a premium, and commercial concerns are sometimes able to wangle space originally assigned to educational exhibits. Since many of the carnival tents look alike, the manager must be certain which tent is for the venereal disease exhibit. It should have been erected before the truck arrives.

Before any unloading is started the secretary of the fair should point out the specific tent to the manager, who should see that the front entrance of the tent has an unobstructed view of the midway. If such is not the case he should immediately consult with the secretary and any concessionaires whose displays are blocking the view. Some sort of understanding agreeable to all parties can usually be reached.

The manager should also call the health commissioner to advise him that the show has arrived and is about to be set up. Most health officers come to the fairgrounds to see if there is anything he or his staff can do to assist. Our unit is self-sufficient, however, and if necessary can operate without any local assistance.

While the helper is unloading the truck and erecting the front display banner, the manager should secure the services of the fair's electrician, because the three-wire 220-volt alternating current must be broken into two lines, one for the operation of the projectors and the other for the house, display, and front banner lights. Once the electric set-up has been installed and checked, the manager must see that no one taps the line to provide current for some other purpose. If a clear line is not available, fluctuation in power can cause inferior projection and sound.

Next, the men set up the display panels, chairs, and information booth. The projectors and screen are set up and tested for sound and focus. The literature to be distributed on opening day is arranged attractively at the information booth. When every detail of the show's installation and operation has been checked, the men can relax and wait for the opening-day crowd.

It has been our experience that the best procedure is to start the movies around noon and continue until about 11:30 p. m., at which time the crowd on the midway starts to leave. The films and projectors should be thoroughly cleaned each morning, and the projectors should be oiled periodically throughout the day. The film breaks occasionally The supply of litand must be spliced. erature should be checked and replenished frequently. The tent floor should be kept clean and the rows of chairs straight. The entire exhibit should always be neat and attractive.

The manager should keep in touch with the local health department and should call the State health department in any emergency.

At some fairs the local health department may set up a blood-testing station in one section of the tent. We have found that such programs meet with varying degrees of success. Pleasure-bent fairgoers apparently like to visit the exhibit and absorb some health education, but they are likely to shy away from a blood test. They prefer to see the show, take some literature, and go their way without being singled out as individuals. Some local

health departments provide nurses to distribute literature and answer questions about the venereal diseases. Others provide workers to assist the staff in projecting the films. The entire project is more successful when the local health department is cooperative. A few have loaned projectors, and one arranged for free sawdust from a lumberyard when heavy rains and poor drainage threatened to close the show. The health department staff is always enthusiastic when they look into the tent and see every seat occupied and the entrance jammed with standees. We have played to a "standing room only" crowd during the peak of operation at every fair.

The manager makes hand tallies of persons entering the exhibit in order to estimate daily attendance. He usually counts the number of persons entering the tent during 15 minutes of each hour, so that every hour of the day's performance is represented in the sample. Multiplying these 15-minute counts by 4 provides an estimate of hourly attendance, and the sum of the hourly estimates is used as the exhibit attendance for the day.

Once the fair season starts, the program supervisor from the State health department must work closely with the manager, making frequent trips to the show. Many unexpected things happen. A county fair may be suddenly canceled, for instance, because of a poliomyelitis scare. When a fair is canceled, an attempt should be made to secure a lastminute booking elsewhere. The touring unit must be supplied with replacements for any broken equipment and with a constant flow of literature.

Costs

Table 1 contains a breakdown of the cost of operating one tent show for a season of 10 fairs, assuming that the truck, projectors, and some tools are available from the State health department's stock. The costs shown are liberal and should cover any emergency purchases. If anything, the figures exceed actual expenses.

Table 1.—Cost of operating one tent show for a season of 10 fairs

Operation	Cost
Staff: Supervisor-advance man @ \$300 per month for 6 months Manager @ \$250 per month for 4 months	\$1,800 1,000
Helper @ \$200 per month for 4 months Total	3,600
Rentals: Tent @ \$75 per fair for 10 fairs 60 chairs for season Total	750 150
Other operations: Exhibit construction, including art work Electric equipment Films	1,000 350 500
Literature Gasoline and oil Miscellaneous	2, 500 75 300
TotalGrand total	4, 725 9, 225
Claria (Oval	0,220

Certain items of the equipment, such as the display panels, information booth, and electric wiring system, can be used year after year. Thus, costs of the first year of operation include overhead and are at a maximum. Once the exhibit has been "set" the operating costs are quite reasonable. Careful planning and efficient operation of the program will result in lower costs than those shown. conditions in Ohio, which we assume to be a typical Midwestern State, this show could be expected to attract at least 100,000 persons per fair season. With the costs shown, this would mean an expenditure of less than 10 cents per person exposed to the films and literature.

Multiple-Unit Operation

The Ohio venereal disease tent-show program ran through the 1949 fair season with two units operating simultaneously in different parts of the State. This two-unit system doubled the activity, attendance, and results. In general the system worked well. Unfortunately, we had only one truck to serve the two units and had to employ an extra man who did nothing except serve as truck driver and chauffeur. Week-end operations became com-

plicated, since two tent shows in different sections of the State had to be torn down, loaded into the truck at separate times, and then transported to two new locations. Since the one truck at our disposal could accommodate the equipment and staff of only one unit at a time, limitation of trucking facilities caused many delays, excessive travel, and long hours of work over the week end. The schedules were always maintained, The experience taught us however. that each unit should be self-sufficient and travel with its own truck. than the transportation difficulties noted above. the two-unit operation was successful.

General Observations

- 1. County fairs attract throngs of people representing all walks of life. The visitors are relaxed, have time on their hands, and are looking for amusement. Their only desire is to find "things to do." Since the tent show is a free exhibit offering movies and seats, it is quite attractive to most visitors. Often a whole family visits the exhibit. It is our opinion that the county fair represents an opportunity for health education that should not be overlooked.
- 2. Health commissioners who are interested in strengthening their educational program are enthusiastic about the tent show. As proof of this, 74 county health departments have requested the venereal disease tent show for 1950. Also, every county where the show has played has requested a return booking. Although we cannot fill all these requests, we plan to cover as many county fairs as possible, with priority in booking given to counties where the tent show has not previously played. This policy will be carried out until each county fair has been visited. It has been our experience that repeat dates are very successful and draw larger crowds than at the previous year's showing. However, in 1950 we plan to sacrifice total attendance for coverage of the less populous counties.
 - 3. We believe this health education

technic can be used to disseminate information to the public on any disease problem or any combination of health problems.

4. Although many in the health field are inclined to believe that the public has been saturated with venereal disease education, the demand for literature at the tent show and the number

of persons seeing the films indicate that there is much work still to be done to increase the public's knowledge and to change attitudes toward the venereal diseases.

5. The cost of the tent-show program is reasonable when it is considered on the basis of total attendance and number of pieces of literature distributed.

The Antigens of the Cultured *Treponema Pallidum* (Reiter's Strain) and the Antispirochetal Antibodies in Human Syphilis¹

G. D'Alessandro, F. G. Oddo, L. Dardanoni

The work of several authors shows that serums of patients with syphilis in different stages react strongly with cultured treponema (Reiter's strain of *Treponema pallidum*). There is evidence, shown in the investigations carried out by Turner (1), by Eagle and Hogan (2), and by ourselves (3), that syphilitic serums contain a specific antitreponemal antibody that is different from the so-called reagin, i. e., the antibody responsible for the Wassermann and flocculation tests.

Starting from this point, we have for some years conducted investigations on the antigenic structure of this organism (4,5). For this purpose, the behavior of human syphilitic serums and of rabbit and guinea pig Reiter antiserums against treponemal bodies and their chemical fractions has been tested.

The data obtained show that four different antigens are present in Reiter's treponema:

1. Treponema-specific antigen, which is of proteic nature. This antigen has been extracted by successive freezing and thaw-

1 From the Istitute d'Igiene e Microbiologie

ing of the spirochetes or by treatment of frozen organisms with 1M KCl. Active proteic material can be precipitated from these extracts by salting out with (NH₄)₂SO₄.

The reactivity of the antigen with guinea pig antiserums and with most human syphilitic serums is destroyed by heating for 1 hour at 76° C. However, a residual activity of the heated antigen with rabbit antiserums has been observed; on the other hand, treatment of rabbits with heated spirochetes elicits antibodies which react with "native" proteic antigen.

The antibodies against treponema-specific antigen of proteic nature are definitely demonstrable in almost every case of secondary syphilis and in some cases of primary syphilis, even if the reagin is lacking. Their presence is irregular in the older infections and in treated cases. In some cases of late congenital syphilis, treponemal antibodies are not demonstrable, while the reagin is still present in significative amount.

The deduction suggested is that the presence of this antibody may be an expression of the activity of the infection.

¹ From the Istituto d' Igiene e Microbiologia dell' Università di Palermo.

- 2. Treponema-specific antigen, polysaccharidic in nature, which is obtained through extraction with trichloracetic acid of the spirochetal bodies, previously treated with NaOH 2N. After acid hydrolysis, it releases dextrose and uronic acids. Rabbit antiserums obtained by inoculation of intact treponemal bodies strongly react in the precipitin test with the polysaccharidic hapten. Human syphilitic serums and guinea pig antiserums do not react with this antigen.
- 3. Alcohol extraction of treponema brings out a significant amount of lipoidal ubiquitous antigen, whose identity with the tissue lipoidal antigen has been verified by us. It results that, although the total lipoid contents are equal, the amount of lipoidal ubiquitous antigen is greater in the alcohol or ether spirochetal extracts than in those obtained from the *Bacterium coli* or from the beef heart.

These data suggest that the lipoidal antigen in the spirochetes may exhibit, in consequence of its availability, i. e., its presence in the cell in a form that is antigenically effective ("disponibilität," according to Sachs), a serologic and antibody-forming activity. We maintain our opinion that the reagin is directly promoted by the pathogenic treponema.

4. Witebsky's (6) old data, i. e., that in Reiter's treponema a peculiar antigen is present which is identical or similar to the organ-specific antigen of the brain, have been confirmed.

In our laboratory, two parallel tests for antitreponemal and antilipoidal antibodies are carried out, that is, a qualitative analysis of the two main syphilitic antibodies is performed (7, 8).

It seems that the new procedure will allow remarkable progress in the serology

of syphilis, which until now has been confined to the unilateral study of the reagin only; the reagin, however, is one but not the sole antibody promoted by the *T. pallidum* in the syphilitic organism.

We believe that the relatively purified preparation of proteic treponema-specific antigen of cultured *T. pallidum* (Reiter's strain) offers a practical way to test the presence of spirochetal antibodies in human syphilis.

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CURRENT NOTES AND REPORTS

"The Ever-Handy Clinic"—A New Visual Aid for Students

R. D. Wright, M. D., and D. V. Liberti 2

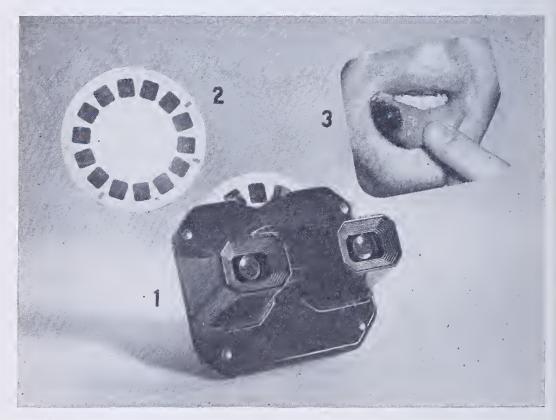


FIGURE 1.—"Ever-Handy Clinic" slide disk. (1) Disk inserted in stereoscopic viewer. (2) Disk containing photographs of seven lesions. (3) Approximate size of picture as seen through viewer.

In the last few years it has become increasingly difficult in many areas of the United States to find material suitable for the clinical study of the venereal diseases. We should, therefore, plan now to develop suitable visual aids for teaching the clinical aspects of these diseases to medical students and others who help in their control.

The Division of Venereal Disease is meeting this problem by instituting a project to produce stereoscopic color slide disks that can be made available to medical schools and to various other professional groups.

These disks (fig. 1), tentatively called "The Ever-Handy Clinic," are designed to fit a stereoscopic viewer ³ that is commercially available throughout the United States. The color transparencies are mounted on easily inserted disks, approximately 3½ inches in diameter, each containing seven views of various lesions of

¹ Senior Surgeon, Chief, Technical Aids and Services Branch, Division of Venereal Disease, U. S. Public Health Service.

² Assistant Chief.

³ Sawyer's View-Master, Portland, Oreg.

the venereal diseases. The stereoscopic viewer has a trigger that moves the pictures into position.

These clinical pictures, with their accurate color and lifelike perspective, are expected to be of great value both to students of venereology and of dermatology. As a professor of syphilology put it recently after reviewing the preliminary slides, "They are almost better than seeing the actual patient." His statement was motivated by the fact that they will give the student time for prolonged study either at school or in his own quarters. The slides will thus virtually bring the clinic to the student.

Because both the viewer and the slide

disks can be purchased for only a few dollars, they should be within the means of any medical school, library, or student.

The photographs for the slides are being made for the Division of Venereal Disease by the Communicable Disease Center's Audio-Visual Production Branch, directed by Mr. Gale C. Griswold. The photographs are of patients at the Alto Medical Center in Alto, Ga., and other treatment centers.

Information about the availability of the slides will be announced soon. Inquiries should be directed to Dr. Theodore J. Bauer, Chief, Division of Venereal Disease, United States Public Health Service, Washington 25, D. C.

CURRENT LITERATURE

ACTA CARDIOL., BRUSSELS

Observations in heart block. Supernormality of A-V and intraventricular conduction and ventricular parasystole under the influence of epinephrine. Alfred Pick and Alfred P. Fishman. Acta cardiol., 5:270–287, Fasc. 3, 1950.

A report is presented of the electrocardiographic findings in a 25-year-old colored woman with almost complete A-V heart block, associated with syphilitic heart disease. Multiple regions of block could be demonstrated as well as the temporary existence of a supernormal phase of recovery in two of these regions.

ACTA MED. SCANDINAV., STOCKHOLM

Aneurysm of pulmonary artery, Reidar Grelland, Acta med, Scandinav., 137: 374-380, Fasc, 5, 1950.

A case report is presented of a 60-yearold man admitted to Aker Hospital, Oslo, Norway, after suffering dyspnea and pain in the chest for 10 years. Angiocardiography revealed a saccular aneurysm of the left branch of the pulmonary artery caused by untreated syphilis.

AM. J. M. Sc., PHILADELPHIA

The substratum of central nervous system manifestations in syphilis. George Wilson, Charles Rupp, Helena E. Riggs, William W. Wilson, and Hal Pitman. Am. J. M. Sc., 220: 84-86. July 1950.

From 1935 to 1940, inclusive, and during 1946 and 1947, at the Philadelphia General Hospital, the authors analyzed a group of 339 neuropathologic autopsies which presented either serologic or postmortem evidence of syphilis. In 176 cases, syphilis was incriminated as a possible factor in respect to the neurologic and psychiatric symptoms. In the remaining 163, pathologic study suggested nonspecific disease as the predominant cause and syphilis as incidental in respect to nervous and mental symptoms.

AM. J. OBST. & GYNEC., ST. LOUIS

The treatment of gonorrhea in women with streptomycin. Arnold M. Salzberg, C. Whitney Caulkins, and Randolph H. Hoge. Am. J. Obst. & Gyncc., 60: 217–220, July 1950

Of 18 women with gonorrhea treated with streptomycin at the Medical College of Virginia, 17 were considered cured. No evidence of streptomycin toxicity occurred.

A study of the trichomonad population in experimentally infected Rhesus monkeys. I. The efficiency of intensive microscopic search compared to culture technique. Mary Hoffman Williams. Am. J. Obst. & Gynec., 60: 224–225, July 1950.

Data obtained from a study of nine female Rhesus monkeys experimentally infected with *Trichomonas vaginalis* show that where the vaginal trichomonads were not demonstrable by intensive microscopic search, the culture technic revealed their presence in the majority of samples. It is hoped that a similar technic used to demonstrate the infection in women will result in greater accuracy in diagnosis and therapy.

AM. J. TROP. MED., BALTIMORE

Laboratory tests with newer antibiotics on microorganisms commonly prevalent in the tropics. Oscar Felsenfeld, Italo F. Volini, Viola Mae Young, and Sachiko J. Ishihara. Am. J. Trop. Med., 30: 499–502, July 1950.

This is a comparative evaluation of penicillin G and other antibiotic drugs in vitro and in experimental animals. Trichomonads were irregularly influenced by bacitracin and neomycin. Two hundred to two thousand units of bacitracin per milliliter medium were necessary to inhibit the growth of five strains. *Trichomonas vaginalis* was resistant to bacitracin and neomycin.

AM. PRACT. & DIGEST TREAT., PHILADEL-PHIA

Emergency psychotherapy in general practice: the psychotic patient. Wilfred C. Hulse and Louis Lowinger. Am. Pract. & Digest Treat., 1:706-716, July 1950.

The authors consider the aims and objectives of a program of emergency psychotherapy with various types of psychotic patients, including those with general paresis.

ANN. SURG., PHILADELPHIA

Arterial aneurysms. Barton McSwain and Walter Diveley. Ann. Surg., 132: 214– 224, Aug. 1950.

Of 26 patients with arterial aneurysms subjected to operation in the Vanderbilt University Hospital since 1925, 7 had positive Wassermann or Kahn reactions. There was no absolute evidence in any that syphilis caused the aneurysm, since the *Treponema pallidum* was not demonstrated in the microscopic sections of the sac. Of the three who died, two had cerebral hemorrhage and one coronary occlusion.

ARKANSAS HEALTH BULL, LITTLE ROCK

VD instruction given white high school students. Arkansas Health Bull., 7: 2, Apr. 1950.

Informal lectures, discussions, and visual education are used in a new venereal disease control program particularly adapted for teen-age groups. High moral standards are stressed as the best method of preventing the spread of venereal disease.

Brit. J. Ophth., London

Experimental study on the efficiency of different substances in retarding the absorption of penicillin introduced into the subconjunctival spaces. Giuseppe Lepri. Brit. J. Ophth., 34: 425–430, July 1950.

At the Eye Clinic, University of Pisa, Italy, a study was made of the effectiveness of different substances possessing a local retarding action, on absorption of penicillin introduced subconjunctivally. It was found that penicillin-procaine and penicillin-adrenalin combinations are of the greatest importance, as being the most active in retarding the absorption of the antibiotic and in giving higher and more prolonged intraocular levels.

Bull. Georgetown Univ. M. Center, Washington

Recent advances in dermatologic therapy.

Maurice J. Costello. Bull. Georgetown
Univ. M. Center, 4:8-13, June-July 1950.

In this general review the author presents a brief outline of recent treatment measures of various infections, including condylomata acuminata, granuloma inguinale, and arsenical dermatitis.

BULL, WORLD HEALTH ORGAN., GENEVA

Lymphogranuloma venereum. A general review. Waldemar E. Coutts. Bull. World Health Organ., 2: 545-562, No. 4, 1950.

History, epidemiology, and etiology are discussed. Clinical manifestations observed during the three stages are given in detail, and importance of differential diagnosis is stressed in case of tertiary syndromes. Best results are obtained with aureomycin.

Complement-fixation reactions with cardiolipin antigen compared with Kahn reactions. A. Bekierkunst and F. Milgrom. Bull. World Health Organ., 2: 687-688, No. 4, 1950.

A study on 2,546 serums permitted a comparison between a Wassermann complement-fixation test, employing cardiolipin antigen, and the standard Kahn test, utilizing Kahn antigen. This work, done in Poland, showed complement-fixation test was at least as sensitive and specific as the Kahn test.

Survey of venereal diseases in Afghanistan. J. C. Cutler. Bull. World Health Organ., 2: 689-703, No. 4, 1950.

Survey of conditions made by the author shows lack of equipment and supplies for diagnosis, laboratory work, and treatment. Recommendations made included establishment of diagnostic services in hospitals and clinics of Kabul and a penicillin-treatment program.

CLIN. J., LONDON

The eye in relation to general medicine and neurology. S. P. Mcadows. Clin. J., 79: 113-124, May 1950; 141-148, June 1950.

This is a general article which discusses causes and effects of various dis-

eases or conditions of the eye, among which are syphilitic optic atrophy and syphilitic ocular palsies.

Connecticut M. J., New Haven

The use of Chloromycetin. Marvin B. Day. Connecticut M. J., 14: 417-419, May 1950.

Review of literature on effectiveness of drug in treatment of various diseases including lymphogranuloma venereum is presented. Good clinical response has been reported in one case of lymphogranuloma venereum.

DELAWARE STATE M. J., FARNHURST

Mikulicz's syndrome. Report of two cases, George B. Heckler. Delaware State M. J., 22: 143-145, July 1950.

The symptomatology, pathology, and etiology of this disease arc discussed. Two cases are reported. The first involved a 34-year-old colored female in whom the disease was secondary to syphilis and who responded dramatically to antisyphilitic therapy. The second case concerned a 24-year-old colored female in whom the disease may have been secondary to syphilis or tuberculosis and who has shown no local recurrence after surgical excision of one involved gland.

FERTIL, & STERIL., NEW YORK

The treatment of male infertility. Fred A. Simmons. Fertil. & Steril., 1: 193-198, May 1950.

Infections causing sterility are usually venereal. Of 536 husbands studied, 24 had blockage of the accessory sexual apparatus due to bilateral epididymitis or vasitis of venereal disease origin. The treatment of this group is strictly surgical.

HEALTH BULL., RALEIGH

Syphilis research laboratory. Departmental reports. Health Bull., 65: 15-17, June 1950.

Combined activities of the Reynolds Syphilis Study Program and the United States Public Health Service are disHEALTH BULL., RALEIGH—CONTINUED cussed. Research projects discussed are those of treponemal immobilization.

Division of Epidemiology and Vital Statistics. Departmental reports. Health Bull., 65: 18-21, June 1950.

Granuloma inguinale reached a new record of 66 cases in 1949. Gonorrhea steadily increased since 1935 to 16,107 cases. Chancroid has steadily declined since 1943. Syphilis reports for 1949 totaled 6,748.

INDIAN J. VEN. DIS., BOMBAY

Serologic patterns in syphilis. John C. Cutler. Indian J. Ven. Dis., 16: 49-59, Apr.-June 1950.

Serologic changes observed in penicillin-treated syphilis before, during, and after therapy as reflected by a battery of standard tests for syphilis are discussed.

INDIAN M. GAZ., CALCUTTA

Gonococcal arthritis. S. L. Malhotra. Indian M. Gaz., 85: 187-188, May 1950.

Results of treatment of 46 smear-positive patients are reported. It is suggested that a preliminary course of streptomycin to eliminate the secondary organisms found in prostatic secretions may completely dispense with pyretotherapy as an essential part of treatment thus simplifying the treatment of gonococcal arthritis.

Experience with Flocillin "96," M. Dutt and P. N. Bardhan. Indian M. Gaz., 85: 199-202, May 1950.

Therapeutic efficacy of Flocillin "96", a suspension of procaine penicillin G in peanut oil and aluminum monostearate, has been tested in 29 cases including 7 of gonococcic urethritis and 1 of gonococcic vulvovaginitis. Minor disorders such as common cold, simple abscess, and gonorrhea can be cured by one injection while maladies of serious nature might require repeated injections at 48-hour intervals.

Irish J. M. Sc., Dublin

Clinical aspects of Chloromycetin. J. Stanley White. Irish J. M. Sc., Sixth Series: 326-332, July 1950.

In this general review the author includes the chemistry, therapeutic range, dosage schedules, blood-serum levels, and mode of action of the drug.

J. BACT., BALTIMORE

The growth of the Reiter strain of Treponema pallidum in the chick embryo. William B. Beardmore and Matt C. Dodd. J. Bact., 60: 5-7, July 1950.

Reiter strain of *Treponema pallidum* was cultivated in embryos of paraffincoated hens' eggs. Experiments showed that the Reiter strain can be cultivated in chick embryos if anaerobic conditions are provided.

Nutritional requirements of treponemata. II. Pantothenic acid, glutamine, and phenylalanine as additional growth-promoting factors for the Reiter treponeme. Harry G. Steinman and Harry Eagle. J. Bact., 60: 57-68, July 1950.

Present paper shows that an enzymatic protein digest is a complete replacement for the thioglycolate medium and that its growth-promoting activity is due largely to pantothenic acid, glutamine, and phenylalanine. When these were added in optimal amounts, the minimal concentration of casein digest necessary for growth was reduced to 1:10,000.

J. BONE & JOINT SURG., LONDON

Osteolytic bone syphilis. Henry McGladdery. J. Bone & Joint Surg., 32-B: 226-229, May 1950.

Case reports are presented of five patients ranging in age from 21 to 32 years, with atrophic bone lesions of syphilis, in which osteoporosis was the striking feature, being much greater than the new bone formation. This is contrary to standard descriptions of syphilitic bone lesions, which emphasize that new bone formation usually exceeds bone destruction.

J. INDIAN M. A., CALCUTTA

Modern treatment and diagnosis methods for control of syphilis. J. Indian M. A., 19: 381–382, July 1950.

Program as carried out by the venereal disease control team at Simla, India, will

J. Indian M. A., Calcutta—Continued serve as basis for others throughout southeast Asia. The team, led by Dr. J. C. Cutler, examined approximately 1,900 persons and ran about 1,500 blood tests. Tests revealed that about 70 percent of the adult population were infected.

J. INSUR. MED., LOUISVILLE

Mortality among patients with mental disease in the New York civil State hospitals. Benjamin Malzberg. J. Insur. Med., 5: 5-13, Dec.-Jan.-Feb. 1949-1950.

This analysis deals with deaths among 21,253 patients on the books of the New York civil State hospitals during the three fiscal years ending March 31, 1949. Syphilis, the second leading cause of death, was responsible for only 6.1 percent of the total.

Gonorrhea in the female. Arthur G. King. J. Insur. Med., 5: 15-17, Mar.-Apr.-May 1950.

The author discusses various aspects of this disease in women, with emphasis on incidence, pathology, complications, diagnosis, and treatment.

Lymphogranuloma venereum and granuloma inguinale. Borris A. Kornblith. J. Insur. Med., 5: 30-32, Mar.-Apr.-May 1950.

The author differentiates between these two diseases, discussing the etiology, pathology, diagnosis, and treatment measures for each.

J. INVEST. DERMAT., BALTIMORE

Aureomycin in the treatment of granuloma inguinale and lymphogranuloma venereum. Virgene S. Wammock, Robert B. Greenblatt, Robert B. Dienst, Calvin Chen, and Robert West. J. Invest. Dermat., 14: 427-434, June 1950.

At the University of Georgia School of Medicine, Augusta, 20 patients with granuloma inguinale and 20 with lymphogranuloma venereum were treated with aureomycin. The drug proved very effective in the treatment of granuloma inguinale. In lymphogranuloma venereum, it was of greater value in the treatment of late manifestations than in the relatively early case with buboes. Dosage and toxicity are discussed.

The treatment of early syphilis with crystalline penicillin G in peanut oil and beeswax (P. O. B.) employing a treatment schedule of 300,000 units given twice a week for a period of 8 weeks. Report of 113 cases. Nathan Sobel, Louis Chargin, Charles R. Rein, and Theodore Rosenthal. J. Invest. Dermat., 15: 13-18, July 1950.

Of 160 patients treated at the Skin and Cancer Unit of the New York University Medical Center, 113 remained under observation for 8 months or longer following termination of treatment and these constitute the basis of this report. The results in primary syphilis, seronegative and seropositive, compare favorably with the 16-day schedule of treatment recently reported, while in secondary syphilis the results are less satisfactory. The twice-a-week schedule lends itself well to ambulatory treatment.

J. Pharamacol. & Exper. Therap., Baltimore

Pharmacology and toxicology of antibiotics.

Hans Molitor and Otto E. Graessle.

J. Pharmacol. & Exper. Therap., 98: 1-60,

Apr. 1950 (part 2).

An extensive review is presented of the pharmacologic properties and toxicity of penicillin, streptomycin, mannosido streptomycin (streptomycin, B), dihydrostreptomycin, aureomycin, Chloromycetin, tyrothricin, streptothricin, neomycin, subtilin, polymyxin, and bacitracin.

J. PHILIPPINE M. A., MANILA

Significance and evaluation of the serologic titer in the diagnosis of syphilis. Ricardo C. Garcia. J. Philippine M. A., 26: 121-124, Mar. 1950.

This is a study of 141 female patients who were examined clinically and sero-logically at the Manila Rapid Treatment Center. On the premise that there is not yet any test which will differentiate true positive from false-positive reactions in the serologic examination for syphilis, the author hopes that this study may pave the way to future attempts at evaluating properly the significance of the results of the Kahn test, by fitting the serology into the clinical history and physical findings.

J. UROL., BALTIMORE

Prostatism in the Negro with clinical and pathological studies. Harvey J. Whitfield. J. Urol., 64: 106-113, July 1950.

A study is reported of 155 cases of surgical prostatism among Negro patients admitted to the urologic service of Provident Hospital, Chicago, over a 5-year period from January 1943 to January 1948. A history of gonorrheal infection was obtained in 140 patients, while the serologic reaction of the blood was positive for syphilis in only 7 cases.

LANCET, LONDON

The experimental background and clinical use of antibiotics. Perrin H. Long, Eleanor A. Bliss, Emanuel B. Schoenbach, Caroline A. Chandler, and Morton S. Bryer. Lancet, 1: 1139–1145, June 24, 1950.

In this general article the authors discuss toxicity, pharmacology, clinical, and prophylactic uses of penicillin, streptomycin, polymyxin D, aureomycin, chloramphenicol, terramycin, and neomycin. The use of these in various infections, including venereal disease, is given in chart form.

M. TIMES, NEW YORK

The newer antibiotics having wide antibacterial spectra. Special Article. M. Times, 78: 298–319, July 1950.

This summarization attempts to cover the essential therapeutic information on chloramphenicol, aureomycin, and terramycin.

M. World, London

The 'one shot' treatment of venereal diseases. R. R. Willcox. M. World, 72:518-523, June 23, 1950.

The author reviews the literature, examining the present position of the various "single shot" treatments in respect to venereal diseases, especially gonorrhea and syphilis.

MINNESOTA MED., ST. PAUL

Advantages and limitations of the quantitative VDRL slide test. Anne C. Kimball and Henry Bauer. Minnesota Med., 33: 573-578, June 1950.

Beginning July 1, 1950, the Minuesota Department of Health Serologic Laboratories plan to report quantitatively blood specimens giving positive VDRL serologic slide tests for syphilis. This test has been studied in the Department of Health Medical Laboratories since October 1, 1949. A summary of results is presented as an indication of the value and limitations of this test procedure.

The cliuical application of quantitative reports of serologic tests for syphilis. Francis W. Lynch. Minnesota Med., 33: 579-581, June 1950.

This article, which is based on the results of studies on specimens submitted to the Minnesota Department of Health from private practice and from Ancker Hospital from October 1, 1949, to April 1, 1950, is presented in the hope of familiarizing Minnesota physicians with the advantages of quantitative reports of serologic tests for syphilis.

NEW ORLEANS M. & S. J., NEW ORLEANS

The eye in diseases of the nervous system. Everett L. Goar. New Orleans M. & S. J., 102: 609-613, June 1950.

Cerebrospinal syphilis is listed among diseases an ophthalmologist may detect in his eye examinations. Author expresses belief he is 95 percent right in attributing the Argyll-Robertson pupil to neurosyphilis.

Heart disease in the Shreveport Charity Hospital. Bryan Harris, W. M. Allums, J. E. Holoubek, and Alice Baker Holoubek. New Orleans M. & S. J., 102: 613-616, June 1950.

A statistical survey of 238 autopsies of cardiac deaths at the hospital between 1944–1948, inclusive, is presented. The second most common etiologic cause of the cardiac deaths was syphilitic heart disease.

NEWS, CHAPEL HILL

\$175,000 V. D. Laboratory officially opens. News, 5: 1, 6, Summer 1950.

Function of the new venereal disease laboratory at the University of North Carolina is to conduct research in venereal disease problems and to study syphilis and immunity to syphilis through experiments on rabbits, rats, and other animals. Evaluation of new tests for NEWS, CHAPEL HILL—CONTINUED syphilis will be made, as well as attempts to produce a vaccine to immunize large numbers of people.

PROC. ROY. SOC. MED., LONDON

Macular atrophy in syphilis. B. Schwartz (for H. W. Gordon). Section of Dermatology. Proc. Roy. Soc. Med., 43: 562-563, July 1950.

A case report is presented of a 57-yearold male who was first seen in November 1949 in the Venereal Disease Clinic at St. George's Hospital during routine investigation of his pregnant wife's positive Wassermann reaction. The case is presented as one of macular atrophy, an uncommon manifestation in syphilis. Antisyphilitic treatment caused rapid disappearance of the lesions on the feet and arm, but has had no effect on the atrophic lesions on the back.

PUB. HEALTH LAB., OLEAN

Neglected considerations in the study and control of serologic inconsistencies. Paul Fugazzotto. Editorials. Pub. Health Lab., 8: 42-44, Mar. 1950.

The author states that difficulties in performance of serologic tests lie in inherent weaknesses and deficient descriptions of test technics further complicated by failure in many instances to apply the technics satisfactorily to the testing of specimens in groups of 20 or more. While reference tests are undoubtedly desirable, only after necessary adjustments have been made in the present order, will such tests prove their value.

Use of merthiolate as a preservative for blood specimens on syphilis serology evaluations. Edward L. Reed. Pub. Health Lab., 8: 65-67, May 1950.

A study was conducted to determine the value and limitations of merthiolate. A final concentration of merthiolate of 1:2,500 in pooled serum specimens for intrastate evaluation seems desirable because it is highly bactericidal and well below the concentration which gives anticomplementary reactions by the Eagle-Wassermann test and probably for any of the approved complement-fixation tests

under time and temperature conditions ordinarily associated with the shipment of such specimens.

QUART, BULL, DEPT, OF HEALTH, NEW YORK

Proper handling of specimens. Quart. Bull.
Dept. of Health, 18: 25-29, Summer 1950.
Mazzini slide flocculation test is used
for testing serums. Reactors are further
tested by Kolmer complement-fixation
and VDRL slide tests. Serology report
is made on the same form filled out by

and VDRL slide tests. Serology report is made on the same form filled out by the physician and returned to him by mail. A photostatic copy of the report is kept in the laboratory.

QUART. BULL., NORTHWESTERN UNIV. M. SCHOOL, CHICAGO

Syphilis of bone. Virgil R. May and Louis W. Breck. Quart. Bull., Northwestern Univ. M. School, 24:93-99, Summer 1950.

The literature is reviewed and the authors discuss the pathologic aspects of congenital and acquired syphilis, together with a classification of the lesions. The diagnosis and treatment of osseous syphilis are considered. Case reports are presented for three patients—one with early congenital osseous syphilis and two with late acquired syphilis of the bone.

STAT. NAVY MED., WASHINGTON

Venereal disease contact investigation. Second quarter—1949. Stat. Navy Med., 6: 2-7, Apr. 1950.

Results of civilian health agency investigations of contacts in both continental United States and foreign areas are presented in tabular form. The Navy Venereal Disease Contact Report was designed to provide information to the civilian health agencies for locating and treating contacts.

Today's Health, Chicago

The half-century mark. The venereal diseases. William F. Snow. Today's Health, 28: 64-65, July 1950.

The advances made since 1900 in the diagnosis, treatment, and prevention of the venereal diseases are reviewed.

STATISTICS

Cases of Syphilis and Gonorrhea Reported to the Public Health Service by State and Territorial Health Departments, April-June 1950

[Known military cases excluded]

Symbilis	Late and late latent	Ratio to prior quarter	All vate sources sician sources	0.91 1.20 50 1.12 1.21 12 1.13 (*) 6 1.78 1.38 14 (*) (*) 5 1.81 1.00 11 (*) (*) 2	1.08 1.21 284 1.17 (*) 2 1.14 1.26 45 1.10 1.26 152 1.11 1.40 115 1.98 .77 85 1.19 .86 37 1.99 (*)	1.00 .90 282 1.12 (*) 13 1.98 .63 74 1.00 .59 87 1.11 1.44 71 2.88 39	1.05 1.10 317 1.12 .88 59 1.12 1.45 86 1.00 1.01 1.72	1.08 1.15 21099 1.0498 52 1.35 1.50 54 1.7 1.28 1.1 1.14 3.7
V.	Late and		Total all sources	482 90 193 31 88 88	6, 769 4, 607 3, 868 1, 184 730 168	2, 239 461 643 493 313 463 359	3, 845 477 1, 234 2, 134	2, 796 1, 591 833 636 217 352
	Early latent	Ratio to prior quarter	Total all vate sources sources scienaries	154 0.85 0.88 68 1.13 1.00 26 (*) (*) (*) 44 (.58 (.5) (.5) 11 (.5) (.5) 4 (.5) 4 (.5) 4 (.5) (.5) 4 (.5) (.5) 4 (.5) (.5) 4	2, 228 .90 1.09 36 .65 (*) 1, 036 .97 1.15 981 .97 1.15 497 .80 .79 1.26 .80	1, 71090 1, 08 20592 (*) 27191 (*) 16791 (*) 56881 1, 05 459 1, 17 1, 43 20777	1, 741 1. 00 1. 07 207 1. 01 . 81 513 1. 15 1. 38 1, 021 . 94 1. 02	1, 183 . 96 1, 08 780 . 89 1, 04 290 1, 07 1, 09 23 (*) (*)
	secondary	Ratio to prior quarter	Pri- vate phy- sician sources	9	1.01 22 (*) (*) (*) (*) (*) (*) (*) (*) (*) (*)	83 (**) (**) (**) (**) (**) (**) (**) (**		20 1.08 11.08 11.124 (*) 11.01
1	Primary and seco		Total all sources sources	144 25 (*) 46 1.31 46 1.00 3 (*) 20 (*)	741 .84 22 .65 90 .77 392 .88 338 .92 237 .82 166 1.30	783 43 154 154 295 195 195 195 196 196 196 197 197 198 198 198 198 198 198 198 198 198 198	428 . 79 96 . 83 137 . 81 195 . 75	610 .86 397 .84 206 .72 125 .91 11 (*)
	ij	Federal Security Agency Regions security Agency Regions		111111		1 1 1 1 1 1 1	1 1 1 1	

1.10 1.10 1.39 1.39 1.02 1.02 1.99	. 99 1. 38 1. 17 1. 17 (*)	. 97 1.12 50 . 50 . 46 . 62		. 958 	ı	. 97	16.	
1.06 1.27 1.27 1.27 1.99 1.17 1.17 (*)	. 85 1. 02 1. 15 1. 17 (*) 1. 07	1.00 .88 .88 .89 1.00	. 96 85 1. 28 (*) (*) (*)	. 96 . 80 . 99 . 96 . 10 . 70 . 70 . 89 . 89 . 1. 10	.83	86.	86	
21, 016 1, 080 3, 822 3, 451 3, 272 2, 219 5, 462 1, 671 3, 39	1,860 1,147 312 1,112 621 195 195 31	11, 374 1, 087 2, 636 157 1, 278 6, 216	222 124 124 27 27 20	5,856 384 4,620 1,670 546 63 117 171 130	126	70, 147	72, 284	
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1, 37 1, 42 1, 37 1, 30 1, 30 1, 54 1, 27 1, 25 1, 25 (*)	1.08	1. 10 1. 14 1. 18 (*) (*) 1. 08	#EEEEE	£ £ £ £ £ £ £ £ £ £ £ £ £ £ £ £ £ £ £	€	1, 19	1.20	
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16 (*) (*) 2.02 1.25		. 74 . 97 1. 17 (*) 1. 16	1.04	1: 12 1: 20 1: 20 1: 20 1: 20 1: 30 (*) (*)	ı	1.04	1.04	
1.31 1.15 1.99 2.37 2.37 1.07 1.31 (*)		. 95 1.12 1.12 1.11 1.11		1.03 1.03 1.03 1.13 1.13 1.13 1.09 1.09 1.09	62.	1.07	1.08	
7,098 1,150 1,150 2,524 555 562 782 7	1,572 271 347 807 377 104 17 26	3,660 1,007 1,150 99 511 893	234 107 82 17 11 11	2,480 206 1,888 1,888 197 197 111 111 124 36	54	30, 321	31, 229	
32 96 93 (*,93 28 1.10			85.55.5	1.05	I	96.	96.	
1.08 1.51 1.51 1.51 1.51 1.14 (*)			8,8,0000		(*)	.95	96	
5,513 1,028 505 949 678 678 946 678	686 122 122 377 192 53 26	2,503 580 709 106 180 928	111 50 18 25 8 10	758 200 200 455 150 55 6 6 81 37 37	20	15, 593	16, 607	
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	(*************************************	78 .81 1.67 .67 .65	4.53 (C. C. C		*	88.	86	
1,895 441 441 184 1184 1184 164	396 77 200 83 17 24	991 176 342 47 75 351	66 26 18 18 11	372 772 743 745 711 72 74 74 74 74 74 74 74 74 74 74 74 74 74	10	6, 276	6, 436	
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Estimated.
 *Ratio not calculated when base is less than 30.
 -Ratio not calculable. Base is zero or unknown.

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